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THE REACTIONS OF CHILDREN AND YOUTH TO WARTIME

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THE reactions of children and youth to war depends first of all upon the attitudes of adults in general and parents in particular toward the impact of war upon their daily life. The subject may be opened then by a discussion of the civilian requirements of war and the general reactions of individuals to a war emergency.

In times of war it is necessary to give up much of the independence enjoyed during peace. In a national emergency, such as the present one, submission to authority is essential to good civilian as well as military morale. Time, energy, money, and effort ordinarily devoted to personal interests are directed to the national cause. There is satisfaction in the cooperation induced by a common cause with everyone working together. The united effort tends to eliminate competition and many of the false values of life. On the other hand, personal morals and morale may be lowered by the resulting expression of hates and desire to destroy which cannot be voiced in times of peace and may not then even exist. The disruption of homes and uncertainty as to the duration of the war make it difficult to plan for the future. The life of everyone during such a time is subject to change without notice. These conditions stimulate anxiety in the minds of all parents, not so much because of concern for their own well-being, but because of the threat to the lives and future welfare of their children.

Even though we have had but a short time to observe children and youths in this country since the beginning of a war that has as yet

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This paper has the approval of the Committee on Mental Health, the American Academy of Pediatrics. It is meant to be a summary of the ideas and material available on the subject rather than an original paper. The following references were used freely in preparing it: (1) Parents in Defence: A preliminary report of a committee appointed by the Children's Bureau, Department of Labor; (2) Preliminary Report of Committee on Psychological Problems in War Time, Institute for Psychoanalysis, Chicago; (3) Children in War Time, Parents' Questions, Child Study Association of America, 1942; (4) Civilian Morale in Time of War and Preparation for War, Karl A. Meninger, M.D., Bulletin, Meninger Clinic, Sept. 1941; (5) Child Guidance Twenty Years After, Bernard Glueck, The Nervous Child, No. 1 (Winter), 1941-42; (6) Suggestions to OCD Personnel for Talk on Morale, Jules R. Masserman, M.D., Mental Health Bulletin, Illinois Society for Mental Hygiene, November-December, 1941; (7) Study of Attitudes of 100 Normal Children Toward the War by the author.

hardly touched our shores, we can accurately predict the way they will react to various phases of the emergency. From our knowledge of mental health and the factors that affect it we can predict the reaction of children to the conditions that may arise. Furthermore, we have access to reports from other parts of the world, especially England, where studies have been made of children under the trials and hardships of war. These studies indicate that the effect of war upon the minds of children depends upon the attitudes of parents, the age of the children, and the degrees of mental health previously enjoyed by the children, as well as the dangers, risks, and disruption of normal life which each one experiences. It is important to recognize these reactions of children, because if they are understood much can be done to alleviate the harmful effects of war upon young minds.

In accounting for their own attitudes, parents are confronted with the facts that no one knows the length to which we will have to go to win this war, and that we are certain that the life of every individual will be affected by it. It is also certain that the total war we are embarked upon will bring trials and mental distress to everyone. These conditions stimulate fear. For their personal peace of mind as well as for the morale of the family it is better for parents to admit their fears. Everyone is frightened at the present time and it is nothing of which adults or children should be ashamed. Actually it is a desirable state of mind, because it stimulates effort, promotes alertness, and with its close ally, resentment, aids determination.

Parents should appraise the immediate situation in which they find themselves. First they should see to it that they and their families are animated by a singlemindedness directed to the national aims and the support of the government in its determined efforts. Then they should adjudge the war situation in their own community and home in order to determine as nearly as possible the probable risks, dangers, and changes in routine that will take place, so that precautions can then be taken and plans can be made for eventualities which may come. By these means parents can gain a clear idea of the common goals and plan efficiently for the part they will as individuals probably play to make them attainable.

The attitude of children toward the dangers of war is determined in a large measure by the morale of their parents. Children can "take it" if their parents can. Parents establish good family morale when they recognize unreservedly the possible risks and dangers and discuss them openly with their children to the extent of each child's ability to grasp their significance, and when they give their children the assurance that, come what may, the members of the family will stand by one another until the end. We are all familiar with an analogous situation when a child has to go to the hospital for an operation, for example. He is far less frightened if his parents explain to him exactly what will happen

and assure him that they will be at the hospital with him at the time of the operation and see that everything is done properly until he is well again. Parents cannot protect their children from life but they can help them face it. Neither is it possible to deceive children and keep information from them. Youngsters detect the thoughts and feelings of the adults with whom they are closely associated and are affected by them far more than we think. Uncertainty in their minds as to what is worrying their parents stimulates more fears than the facts themselves. It is far better, therefore, for parents to discuss with their children even the details of the war situation rather than to remain silent, because it is easier for children to accept unpleasant facts from those in whom they have security than from someone outside the family. The certainty of reduced income, the probable curtailment of education, the possibility of brothers or fathers entering the army, of fires and of bombings, and the fact that some people will be killed in the war should be taken up with them. The discussions should include planning for meeting the various situations should they arise. When plans are made with them, children respect their parents, have faith in their honesty, and have confidence in themselves that they will be able to meet an emergency with the help of their parents.

The fact cannot be overemphasized that children imitate their parents. The family program should continue as nearly as possible according to the normal routine. Parents cannot eliminate all radio war programs and war news. It is better therefore to discuss the progress of the war with the children. At the same time parents should be alert to unfounded rumors and often innocent but malicious propaganda which tend to create fear, suspicion, and uncertainty, and therefore undermine morale. Emotionally stable parents can set an example in rejecting information of this kind, and their children will follow the example. Also, children react to serious situations, even death, in the same way as their parents. If they see their parents carrying on, they will do likewise.

As has been pointed out by those who have studied the reactions of children in England to war, there is a distinct relationship between their mental health and their reactions to the trials of war. Those children who had security in their parents and home and who were free from anxieties before the war have shown remarkable ability to meet extreme dangers, while those with a previous history of insecurities and anxieties have shown increased anxieties and more severe reactions to bombings, removal from their homes, and other difficult situations.

Let us now consider the factors which stimulate anxieties in the minds of children during war, recognizing that those of all ages are affected. Infants from birth respond to the attitudes of their parents. The effect upon the young baby of apprehension in the mother is observed frequently by every pediatrician.

Preschool children are most frightened when they are separated from their parents. They have shown the greatest anxiety in cases of evacuation from their homes and when they have been separated from their parents during blackouts. Small children have no conception of war and are unable to understand most of the discussion they hear about it, but they are not especially disturbed by it unless adults are unduly apprehensive. To them Hitler is analogous to the ghost, bogeyman, robber, and other supermen or supernatural symbols that take children away and kill them in their dreams and make them feel frightened while they are awake. As expressed by one bright 5-year-old boy who was mimicking his father with improvisation of his own, "We got to win; we don't want the Germans to take our country." He was told that we did not think the Germans could take our country but he continued, "They would probably kill us; they might hang us." Later on he added, "I bet you my father would kill 'em if they came to our house." In this statement we see his real protector; namely, his home and father.

We must remember that small children can think only in terms of simple concrete associations. This boy for example had little conception of war or its implications. His intellectual ability was demonstrated when a few minutes later he asked, "How old are you?" He was asked to state how old he thought I was. He said, "Seven?" "No." "Fourteen?" "No." "Twelve hundred?" When children are so young that they cannot grasp the seriousness of a situation that they feel in anxious parents, their insecurity and fears are increased.

Children of school age retain the apprehension of previous years but have reached the period of mental growth which enables them to visualize the dangers more concretely. These older children think more about bombings and imagine more specifically what might happen to them and other members of the family. They are afraid of being killed by bombs and are anxious lest their father enter the army and get killed. The possibility of being deprived of food, heat, light, clothing, and their homes is of real concern to them.

According to the experience of the British, there are fewer serious anxieties during the ages of 8 to 12 years than in the preschool or adolescent periods. During this gang period, youngsters like to dramatize events in life, and even though frightened, they like the idea of war. The very fact that they can act out their feelings relieves them of a part of the tension. They are old enough to understand yet are spared the comprehension of the real risks of the older group.

In the adolescent group we find a continuation or renewal of the anxieties of childhood added to the problems peculiar to their age level. During war these problems are more serious, and their anxieties are greatly increased. Everyone will agree that a large part of the hardships of war fall upon youth. They are expected to grow up more rapidly; their education, vocation, marriage, and plans for the future

are uncertain; and a great many of them are faced with attitudes toward life, both within and outside the home, which are diametrically opposite to the teaching they received during their whole childhood. All of these conditions cause anxieties of varying degrees of seriousness.

The shortage of manpower and the large increase in the number of defense jobs paying comparatively high wages together with the need for millions of young men for the army makes it necessary to hasten the growing up of youth; in fact they are commonly "put on their own" before they have the physiologic growth and emotional maturity to accept the responsibilities given them. The early freedom from supervision and sudden acquisition of independence with good wages often finds them without sufficient self-reliance to manage themselves. As a result they are often confused, reckless, and more than normally liable to get into serious difficulties.

There is also a conflict in the mind of youth because the war has suddenly forced upon them attitudes and a philosophy of life quite foreign to the principles they have been taught. There are some who feel that youth has been slow in responding to the national emergency. In so far as this is true, it is an example of the common practice of rearing children to live and think in one way while expecting them to respond in the opposite manner when they are mature. For twenty-five years children have been taught that war is wrong. This attitude reached its height with the pledge against war which was popular a few years ago among college students in England and the efforts of the National Parent-Teacher Associations in this country to bar the sale of toy pistols to children. Now youth is expected to reject all of this teaching quickly and accept war. In some communities there is a law against shooting sparrows, and children are taught it is wicked to kill them. Those who kill the most Japs, however, are national heroes. It is obvious that our teaching has been unrealistic and has resulted in anxieties and confusion in the minds of young men and women. If we are to continue teachings of this kind, then boys and girls should be taught to differentiate between ideals and reality. Striving toward the elimination of war is a worthy goal, but there are no indications of an impending utopia.

Further anxieties are found in the minds of young men and women because of uncertainty regarding opportunities for them after the war is over. Youths, especially during the past thirteen years, have been hearing would-be prophets predict inflation, national bankruptcy, and the end of opportunity in America. These reports have been disturbing to adolescents.

We have described the anxieties in the minds of children of various ages. Now what behavior changes may be expected? The changes in behavior because of the anxieties created by the war vary with the age of the child. As stated before, infants respond to the anxieties of their parents, especially of mothers, by restlessness, crying, and unhappiness.

In the preschool children there are usually irritability and disobedience; there may also be night terrors, enuresis, stammering, or negativism. School children may respond by expressing their fears and demanding frequent reassurance. Other signs of their anxieties may be poor school work, compulsive stealing, and vandalism. Sometimes these insecure, frightened youngsters are very difficult to manage, become tyrants at home, and are examples of the popular misconception of "spoiled children."

Sometimes the reactions of children to removal from their homes and exposure to bombing are extreme. Such behavior has been described by Mons* in these words: "Previously good and intelligent children become suddenly obstreperous, destructive, mischievous, unmanageable in the billet to which they have been evacuated. In some cases the teacher of the new school expresses doubt about the pupil's mental normality when the previous report has shown him to be of scholarship standard. These children reveal as their foremost symptom a strange inability to occupy themselves in their free time. Their behavior implies deep resentment against the adults who have failed to provide security and protection and the collapse of the values which education has carefully built up so far. Death has become a personal problem, and parental authority is no longer a safe shield against this direct threat of extinction." Other reports from England are that children who are kept at home sleep through bombing at night and have little unfavorable emotional reaction. These reports would seem to emphasize the importance of keeping children at home where they have security.

Adolescents react to anxieties by neurotic complaints, abdominal distress, choking spells, and trembling when called upon to recite in class, or by truancy and delinquency, the most serious being sex delinquency.

We have already indicated the general measures which may be taken to minimize the effects of war upon the minds of children. Let us now consider the specific means of aiding them. Children can be given a great deal of help and their anxieties lessened by adapting their emotional needs to the conditions of war. As previously stated, the morale of parents determines the mood of infants. Young children can be relieved of anxieties in proportion to the security they feel in their parents and home. Every effort should be made to keep them with their parents. In case of fires, blackouts, and bombings they feel safe only when they are very close to them. To avoid the loss of parents in blackouts, it has been suggested that children should be tagged so that their identity can be quickly determined. When father is away from home, part or all of the time, mother can give the children security if there is a well-thought-out and organized plan whereby everyone knows what to do in case of emergency and if the children are made to know that mother will be there to see that everything is all right. In the absence of both parents

*Mons, W. E. R.: Air Raids and the Child, Brit. M. J. 2: 625, 1941.

children can be made to feel certain that a mother substitute knows exactly what to do and that they can be close to her in case of emergency.

"If you want to encourage a child to be brave," says Glover* in a recent book on morale, *The Psychology of Fear and Courage*, "you do not begin by telling him that he is silly: you encourage his sense of responsibility, give him something sensible and useful to do, show him a good example, tell him the truth, admit your errors and be friendly with him. He will do the rest himself." It is better not to indulge in a great many drills; children do best if given a few simple directions and enough responsibility to feel they play an important part in meeting an emergency.

Children of school age may be relieved of a part of their anxiety in various ways. There is much relief in a free expression of thoughts. They feel better if they know all about air raids and bombings and can talk about them. War games, supervised to prevent children from actually injuring one another, are valuable emotional outlets and should not be discouraged. Boys and girls like to feel important and to believe they are a part of the defense program, and this expression may be fostered by buying stamps, collecting materials, doing messenger work for officials, and doing Red Cross work. It is important for them to do these things but only during their spare time and while the home is running on a normal schedule, as far as possible. Surely there is no reason for shortening the school year or dispensing with any part of the curriculum for the sake of war activities.

A great deal can be done for the adolescent group by giving them moral support, helping them with their problems, and supplying their emotional needs. Boys and girls of this age need security in their parents, home, community, church, and nation as badly as at any other time in their lives. This is especially true in times like these, when their plans for life, even life itself, is uncertain.

The two emotional needs of youth are (1) to feel that there is something they can do well and (2) to know that there is a place in society for them. The importance of training young men and women is even more significant during wartime than in peacetime. Educational facilities, especially for vocational and professional training, can be utilized for the mental health of youth as well as for the war effort. A mechanized army requires trained personnel.

Youths can be made to feel not only that they are important in the country but that they are an important part of the country. American history in school paves the way for the development of love of country and the feeling that this is *my* country and that its future holds an important place in it for *me*. American history could not be revised to conform more closely to the interests of the adolescent mind. Independence

*As quoted by Karl A. Meninger.

and love for adventure are important to them. They should realize that it was rebels who, seeking opportunity and adventure, founded and developed this country. They should be brought to recognize that their first ancestors in this country, whether they came one or ten generations ago, felt the same way about life as they feel today. They can be made to feel that the days of adventure are not over, whether they enter the army or not. The land frontier, it is true, is gone, but the frontiers of science with the possibilities of invention are just beginning to be recognized and offer far greater opportunities for progress in the future than our forefathers dreamed possible.

Boys and girls can be made to understand that this is the best country in the world for the expression of independence, opportunities for adventure, and real hope for achievement. In these ways youths can be brought to identify themselves with the past and be assured of the future, even though economic conditions may be serious. The war will only temporarily interfere with their life program. In the very near future they will inherit the country because they will soon take their parents' place in the world. This then becomes *their* home and *their* country as they assume its responsibilities.

Young men and women can be helped to recognize the demoralizing propaganda which is unwittingly spread by adults, even by some who occupy important positions in society. They should be warned against those who declare that they see approaching the end of opportunity in this country, even the destruction of civilization, and who feel if wealth is conscripted there is nothing left to live for.

The further development and coordination of youth organization will do a great deal to prevent the serious delinquency that has occurred in England. Recreational centers, Y. M. C. A., Y. W. C. A., camps, church groups, Boy Scout and Girl Scout troops, any well-managed organization that gives boys and girls an opportunity to prevent the personal and general moral deterioration that is threatened by war—all these are of great value. Recent surveys have found a lack, to the point of absence, of adequate homes, schools, playgrounds, recreational facilities, or other group activities for children and youths in the rapidly developing new armament districts. Unless provisions for these important essentials for family living are rapidly created, we can expect vandalism, truancy, or delinquency to develop rapidly among the children and adolescents in these areas, and low morale in the adults. There is a pressing need for a well-organized, coordinated youth program in every community. The mental health and morale of close to 50,000,000 children, adolescents, and young men and women under 21 years of age in this country will be influenced by our efforts in these respects.

TREATMENT OF TYPE-SPECIFIC HEMOPHILUS INFLUENZAE INFECTIONS IN INFANCY AND CHILDHOOD

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INFECTONS due to strains of encapsulated *H. influenzae* constitute a serious problem in pediatrics. Their clinical course and outcome vary greatly with the location of the lesions and the age of the patient; hence, recognition of the pathologic potentialities is necessary for a discriminating approach to therapy. Six distinct types of this organism, designated as a, b, c, d, e, f, are recognized. Virtually all of the serious infections in infants and children appear to be caused by type b. The importance of type b *H. influenzae* as a cause of meningitis has been well known to pediatricians since the pioneer work of Pittman in 1931.[1] The role which this organism plays in infections outside the central nervous system has come to be appreciated only within the past few years.

H. influenzae enters the body through the respiratory tract. Our experience indicates that not only rhinitis and pharyngitis but other pathologic changes occur in most children following the introduction of type b organisms. The severe infections, of which bacteremia is a consistent feature, fall into three categories: meningitis, obstructive infections of the respiratory tract, and pneumonia accompanied by empyema in infants under 1 year of age.

This paper deals with the treatment of these forms of the disease; it describes methods for appraising the severity of infection in individual patients and offers a statement of principles which have led to the suggested procedures.

CLINICAL DESCRIPTION OF THREE COMMON FORMS

Meningitis.—H. influenzae ranks among the three most frequent causes of meningitis in children.[2] In many institutions it holds first place. Until recently, *H. influenzae* meningitis was almost invariably fatal. Most of the cases represent what is termed as primary meningitis, developing out of a relatively clear sky, following an unimpressive upper respiratory infection. There is reason to believe that bacteremia occurs in most patients prior to the meningitis. The majority of patients show clinical signs of paranasal sinusitis, but evidence for direct extension from this source is lacking. Purulent otitis media is an unusual forerunner of influenzal meningitis but a very frequent component

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of the infection in those patients who fail to respond to therapeutic measures or in those who have been sick a long time before being treated. We have not encountered a single instance of proved *H. influenzae* purulent otitis media in the patients who recovered. Its presence is therefore a sign of poor prognosis. Autopsy evidence suggests that the pathologic process has been a generalized one from the beginning, involving the meninges and their blood vessels and frequently producing encephalitic processes beneath them. It has not been possible in any case to demonstrate evidence of direct extension from the ear. However, in one patient the eighth nerve was shown to be surrounded by gross exudate along its course.

Since the beginning of the recent period when treatment has been more effective than before, the post-mortem findings have been more complex than formerly. Lateral sinus thrombosis with extension into other cranial venous sinuses explained one long-drawn-out case. One patient in whom hemiplegia had developed after twelve days of sulfapyridine therapy and whose illness was merely prolonged by treatment with specific antibody had thrombophlebitis of all veins over the left parietal region and parts of both frontal areas. A 6-month-old baby who died within twelve hours after the beginning of treatment showed hemorrhage over one entire hemisphere and thrombophlebitis of the vessels over one parietal region. In a 3-year-old child who recovered after administration of a large quantity of specific antibody and sulfanilamide the eyegrounds showed hemorrhages throughout the acute stage. Vision was grossly reduced for a period of several months after recovery. One year later the visual acuity was largely restored.

The principal difficulty in the early diagnosis of meningitis in children over 1 year of age lies not in the recognition of meningeal involvement but in the bacteriologic identification of the causative agent. There are no clinical features which differentiate meningitis due to *H. influenzae* from other forms. Fulminating pictures identical with those seen in meningococcus infection, except for the absence of petechiae, are frequently observed. On the other hand we have seen the clinical features of tuberculous meningitis duplicated by *H. influenzae;* between these two extremes all varieties occur.

In infants under 7 months of age it is the perception of meningeal involvement which constitutes the chief problem. The patient's failure to manifest clear-cut signs of meningeal irritation until several days after onset presents a serious diagnostic difficulty and adds to the therapeutic problem, for successful treatment depends in large measure on early application of effective measures. Even under present conditions over 75 per cent of young infants die, in contrast to an 83 per cent recovery rate in the age group above 7 months. Evidence suggests that the advanced stage of the disease and the presence of irreparable damage

at the time therapy is started are responsible for the high death rate. The conspicuous vulnerability of young infants can scarcely be ascribed to characteristics of the infecting agent, for our experimental work has failed to demonstrate any significant difference in virulence between strains recovered from the very young infants and those from older infants and children who respond promptly to therapy. Likewise, there is no immunologic evidence indicative of any lack of ability on the part of younger subjects to utilize antibody administered as a therapeutic measure; the fact that recoveries have occurred in infants under 7 months of age in whom the laboratory examinations indicated a less severe infection is very suggestive that their capacity to utilize injected antibody must be regarded as comparable to that of older patients. In any individual case, however, searching inquiry almost invariably discloses the fact that unexplained fever had been present several days prior to any suspicion of meningitis. These considerations should lead us to reappraise our criteria of meningeal disease in this age group. When the fontanel is widely open and its tension is tested in the well-hydrated infant, experience enables one to detect an increase in intracranial pressure some time before stiffness of the neck or a positive Kernig's sign is found. In fact, the latter signs are highly unreliable in the first few months of life, for they seldom appear before the advanced stage of meningitis. If the fontanel is not open sufficiently for estimating tension, the signs of meningeal involvement are frequently limited to drowsiness, alternating with marked irritability, a high-pitched cry, and a vacant look in the eyes. It is warranted to appeal for more frequent use of lumbar puncture when unexplained fever is accompanied by any suggestion of these features. Except in experimental animals under artificial conditions, evidence for the production of meningitis through a properly performed diagnostic puncture of the subarachnoid space is lacking.[3]

Quantitative chemical analysis and examination of the cellular response of the spinal fluid reveal no features which distinguish influenzal from other forms of pyogenic meningitis. The diagnosis must depend upon bacteriologic and immunologic methods applied to the organisms found. Details of these procedures will be given under the section on Tests Useful in Therapeutic Program.

Obstructive Infections of the Respiratory Tract.—The syndrome of laryngotracheobronchitis was first attributed to *H. influenzae* in 1936 by Lemierre.[4] In 1940 the general features of respiratory obstructions produced by *H. influenzae* infection were described.[5] Recently Sinclair[6] has reported on a group of these cases from New Haven and has described their characteristic clinical features in detail. Our experience at the Babies Hospital parallels his in every respect. The agency of *H. influenzae* in this disease will escape recognition unless the blood be cultured, since routine cultures of the nose, throat, and larynx alone

usually fail to isolate this organism unless there is special interest in looking for it. It is believed that this is probably not an unusual disease, though it occurs less frequently than *H. influenzae* meningitis.

It has been asserted that a single agent, presumably a virus, is the sole cause of all nondiphtherial infections which obstruct breathing by producing inflammatory stenosis of the larynx alone or in combination with other portions of the bronchial tree. There is no evidence in favor of this view. Moreover, regardless of what prepares the way, it seems clear from our experience that the major pathologic changes are due to invasion by one or another of a number of different pyogenic bacteria.

When *H. influenzae*, type b, is responsible for obstructive laryngeal, laryngotracheal, or laryngotracheobronchial infections, the illness presents a characteristic history and the patient a characteristic appearance. The onset is sudden and the course fulminating. The entire length of acute illness in those cases which terminate fatally is usually less than twenty-four hours. Mild fever and difficulty in swallowing, and complaint of sore throat on the part of the older children, make their appearance in the course of an apparently innocuous infection of the upper respiratory tract. Dyspnea starts abruptly and increases within a few hours to such a degree as to make hospitalization imperative. The characteristic picture is that of a prostrated child with dyspnea due to laryngeal obstruction. The temperature is high. Effort on the part of the child to increase the airway produces a dramatic scene, which in some cases takes the form of forcible protrusion of the tongue with each inspiration; other patients hold the mouth widely open during both inspiration and expiration. On examination of the pharynx there is diffuse erythema, often with evident edema, and when the tongue is pressed downward, the enlarged red and edematous epiglottis is easily seen. Direct laryngoscopic examination shows almost complete approximation of the posterior wall of the epiglottis to the swollen aryteno-epiglottic folds. The vocal cords are usually uninvolved and the voice is not impaired. At times the cervical lymph nodes are enlarged. Usually the obstruction of breathing is due almost exclusively to edema of the epiglottis and other supraglottic structures. Hence, the process should be termed laryngitis with epiglottitis and not laryngotracheobronchitis, a term frequently used loosely, unless there is evidence that the process extends well into the bronchi. The obstructive syndrome described has been found in our experience only in association with type b *H. influenzae* infection, and therefore, when observed, suggests this etiology immediately. Bacteremia appears to be a constant feature. Occasionally when the infection extends into the trachea, bronchi, and bronchioles, bronchopneumonia ensues; this is the severest form of the disease.

Pneumonia and Empyema With Bacteremia in Infants Under One Year of Age.—In older children, type b *H. influenzae* may cause pneu-

monia which is clinically indistinguishable from the variety due to pneumococcus. When *H. influenzae* pneumonia occurs in infants under 1 year of age, empyema and bacteremia are common concomitants, and the prognosis is poor because of the subsequent high incidence of meningitis. Lumbar puncture is required when such findings are present in an infant, even if there are no decisive signs of meningitis. It has been emphasized that meningeal infection is difficult to demonstrate early in the course. The causative agent of the lung infection is strongly suspected when type b *H. influenzae* is typed directly from the nasopharyngeal mucus or from cultures prepared by the methods to be described. Isolation of the same organism from empyema fluid and blood cultures confirms the identity of the pathogen.

BIOLOGIC CHARACTERISTICS OF H. INFLUENZAE

Some familiarity with the biology of *H. influenzae* is essential for an understanding of the fundamental principles which we have tried to apply in the therapy of these infections. In 1931 Pittman[1] described evidence which indicates that there is a striking resemblance between the biologic features of *H. influenzae* and those of pneumococcus. Both organisms possess similar chemical structure which endows them with the ability to stimulate a specific chemical response in the body. Their structural and pathogenetic similarity may be summarized by stating that each of these organisms is enveloped by a capsule containing a specific carbohydrate, and in the course of metabolism this substance is excreted into the surrounding medium. The detection of this specific substance through precipitin tests was used by Pittman for the original segregation of various strains of *H. influenzae* into types. Heidelberger's analyses, which confirm those of Goebel,[1] indicate that this capsular component is a polysaccharide. Early in our investigations, in which we employed type-specific rabbit serum by a technique identical with that which Neufeld used for typing pneumococci, we were able to demonstrate that these organisms could be identified by capsular swelling and their type determined in fresh, untreated biologic fluids.*[7] Our observations suggest that, as in the case of pneumococcus, an enzyme is present in cultures which destroys the capsule. After six hours of cultivation on either solid or fluid media, capsular degeneration is evident. These similarities led to the assumption that the knowledge derived from the thoroughly investigated field of pneumococcus could be applied to the treatment of *H. influenzae* infections.

A plan of treatment was conceived, based on the principles found to be important in combating pneumococcus infections. Here it has been shown that the capsular substance is the element of the organism upon which both its type specificity and its power to invade the human body

H. influenzae types a and b diagnostic and therapeutic antiserums are available commercially at E. R. Squibb & Sons.

depend. Since the pneumococcus and other organisms of comparable capsular structure liberate soluble-specific substance into any surrounding substrate in which they are multiplying, it is believed that a therapeutic antibody must first neutralize the free carbohydrate before it can attack the same substance in the capsule of the organisms themselves. The concentration of free specific carbohydrate in the spinal fluid and blood of patients with pneumococcus infections is an index of the severity of the infection. It also serves as a measure of the amount of neutralizing anticarbohydrate antibody necessary for recovery from the consequences of infection. When the infection is of average severity and when the metabolism and multiplication of the organisms are inhibited by chemotherapy, the natural antibody response takes care of this situation. It has been shown that in pneumonia the rise in anticarbohydrate antibody in the blood correlates with crisis, whether spontaneous or induced. There is no evidence that the administration of sulfonamides either to patients or to animals in any way influences the production of antibody by the host;[8] antibody production and recovery are correlated here just as in the spontaneous process. Free antibody elaborated by the host in response to infection can be detected earlier in the course of the disease when the patient is treated with a sulfonamide compound than during spontaneous recovery because it has less antigen or specific carbohydrate to neutralize. It would seem then that in recovery from pneumococcus infections, whether by natural means or as the result of sulfonamide therapy, serum therapy, or a combination of these, antibody is an essential part of the recovery process. All evidence points to the fact that this is true for *H. influenzae* infections as well.

These immunologic features of the pneumococcus demonstrate that the amount of antibody required for recovery differs with the severity of the disease and they suggest that a quantitative approach is desirable. The method of quantitative analysis of the antibody in antipneumococcus serum, whereby the amount of type-specific immune substance in a therapeutic antiserum may be determined exactly and expressed in milligrams of antibody nitrogen per cubic centimeter, represents an important advance in immunologic chemistry.[9] Results of analysis by this method parallel those obtained by mouse protection tests, indicating that it is the anticarbohydrate antibody which is the protective factor.[10] When a single dose of antiserum has been administered, its adequacy may be tested either by the Francis intracutaneous polysaccharide test[11] or by a test of the patient's serum directly for presence of free anticarbohydrate antibody. Observations of this kind permit one to obtain an accurate evaluation of the effectiveness of serum therapy, either alone or in combination with sulfonamides.

The other outstanding advance in the immunology of pneumococcus which has clinical application is the production of therapeutic rabbit

serums and the demonstration of their superiority over horse serums.[12, 13] This knowledge has likewise been applied to *H. influenzae* infections.

Our plan of treatment assumed that one could apply the principles involved in the recovery from pneumococcus infection to infection with *H. influenzae*. Since its introduction into practice, we have been able to demonstrate that our original assumptions were correct. The chemical method of exact quantitative analysis of antibody, developed originally for antipneumococcus serum, has been applied with success to *H. influenzae* rabbit serum by Alexander and Heidelberger.[14] The method used originally by E. R. Squibb & Sons for purifying and concentrating the globulin fraction of antipneumococcus rabbit serum has likewise been used in preparing *H. influenzae* antisera. All experience indicates that after an original dose of antibody has been given its sufficiency to the needs of any given patient with influenzal meningitis may be appraised by finding an excess of antibody in the patient's serum. As would be expected, our experimental evidence indicates that the protective element in the serum is the anticarbohydrate antibody.[15] Results of the therapeutic use of the serum suggest that in this infection as in pneumococcus infections, rabbit antibody is superior to that derived from horse serum.[16] The explanation of the superior therapeutic powers of rabbit pneumococcus antibody is based on two factors. The first is the small size of the rabbit antibody molecule;[17] this property endows it with greater power to penetrate cellular boundaries. The size of molecules of horse and rabbit *H. influenzae* antibody has not been exactly determined, but the evidence thus far indicates that the horse antibody molecule against pneumococcus and *H. influenzae* is of the same order of magnitude. The second hypothetical factor which makes rabbit pneumococcus antisera superior is the absence of a zone of inhibition of protection when an optimal maximal dose is exceeded.[18, 19] This prozone phenomenon does not occur with rabbit antibody, whereas limited experience with equine antibody suggests that such a mechanism operates when mice infected with *H. influenzae* are treated with horse antiserum. The study of one patient, who recovered from a mild form of *H. influenzae* meningitis after sulfanilamide unsupported by administration of antiserum, suggests that when recovery occurs with sulfonamide alone, antibody formed by the host plays a significant part in the mechanism of recovery. The results of treatment in meningitis furnish adequate evidence that antibody must be an essential part of the recovery process in the majority of patients and that the amount of specific serum necessary in a given case depends upon the severity of the infection.

TESTS USEFUL IN THERAPEUTIC PROGRAM

Rapid Methods for Identifying H. influenzae.—When gram-negative rods or coccobacilli along with forms morphologically suggestive of

meningococcus or even streptococcus and pneumococcus (when Gram stains are poor) are seen in stained smears of any biologic fluid, the possibility of *H. influenzae* should be entertained. Direct typing and identification of *H. influenzae* can be accomplished under these circumstances by demonstrating capsular swelling with type-specific diagnostic serum.[7] The technique is identical with that used in the Neufeld method for typing pneumococci.

Concentrated suspensions of nasopharyngeal mucus, obtained by a method previously described,[20] serve as an excellent source from which *H. influenzae*, type b, may be identified directly by capsular swelling. This procedure has been of value in identifying the invader early in meningitis when no organisms were demonstrable on stained smears of cerebrospinal fluid, in type b pneumonia, and in obstructive infections of the respiratory tract, prior to tracheotomy. In severest cases of the latter, confirmation may be obtained by testing the patient's serum for free specific carbohydrate by the method to be described.

If stained smears of a sample of cerebrospinal fluid show no organisms, the fluid is centrifuged at high speed (approximately 2,780 r.p.m.) for twenty minutes and the sediment is examined. If organisms still cannot be found on smear 1 c.c. of the fluid is transferred to 20 c.c. Levinthal broth*[21] in a small flask and 0.5 c.c. to a Levinthal agar plate, in addition to routine inoculation on blood agar. This method is efficient for detecting small numbers of *H. influenzae* which may be typed directly by the above method as soon as growth has become manifest (within twelve to twenty-four hours).

Identification of *H. influenzae* in blood cultures is usually possible within eighteen to twenty-four hours on direct examination by the capsular swelling method.

Tests for Estimating the Severity of H. Influenzae Infections.—The success of anticarbohydrate antibody therapy in the treatment of any infection must depend upon the establishment in the patient of a quantitatively satisfactory relationship between antigen (the soluble-specific substance) and antibody (anticarbohydrate present in the serum). The total amount of antigen free in the body fluids, plus the quantity of the same substance within the capsule of the organisms, represents the amount which must be neutralized by antibody before recovery can take place. A direct measure of antigen is impossible. Only crude evaluation is feasible on the basis of laboratory evidence which measures the concentration in body fluids. Examination of the patient's blood, urine,

Levinthal Stock Broth
To nutrient broth add 10 per cent blood (rabbit, horse or human).
Boil for 5 minutes (gently, until brown clot forms).
Filter through filter paper until clear amber broth comes through.
Sterilize by filtering through Berkefeld or Seitz bacterial filter. Autoclaving destroys essential factors.

Levinthal Broth
Dilute Stock Broth, using 1 part stock to 3 parts nutrient broth.

Levinthal Agar Plates
Use equal parts of Levinthal Stock and 4 per cent nutrient agar.

and spinal fluid for a rough estimate of the amount of soluble-specific substance present should be of value in gauging severity. Over a 1 cm. column of the diagnostic typing serum in a small precipitin tube an equal column of the body fluid under examination is carefully layered by means of a fine capillary pipette. A positive test consists in the formation of a white ring (precipitate) at the interface. Experience of this test with spinal fluid from patients with meningococcus meningitis[22] suggests that the time of appearance of the white ring is an index to the amount of soluble-specific substance present and is therefore a measure of the severity of the infection. The appearance of a ring within ten minutes is believed to represent a severe infection. At present this procedure is being used in early diagnosis and evaluation of severity of *H. influenzae* obstructive infections of the respiratory tract. It is hoped that it will prove of value in determining the amount of antibody needed in individual cases of any severe infection due to this organism.

A somewhat simpler method of appraising the severity of infection in meningitis, based on the determination of the concentration of dextrose in cerebrospinal fluid, is recommended for general use and will be discussed under the section on treatment of meningitis.

Test for Antibody Excess.—After the administration of a single dose of type-specific antibody, the size of which is determined by tests which aim to determine the severity of infection, the adequacy is checked by demonstrating an excess of free antibody. Two methods have been used for this purpose. The patient's serum may be examined for its ability to produce capsular swelling of a suitable suspension of *H. influenzae*.* This procedure is identical with the one used for typing the organism. Here, however, the patient's serum is used in place of the diagnostic serum. The excess of free antibody necessary for recovery is not known exactly. We have chosen an arbitrary standard. It is our aim to establish such an excess throughout the first week that the patient's serum, when diluted 1:10, will cause capsular swelling. The second method of determining antibody excess is based on the use of type b carbohydrate in intracutaneous skin tests. Dingle and Seidman[23] have reported on the value of this method, and our results in several patients suggest a good degree of correlation with the capsular swelling capacity of the patient's serum. One-tenth of a cubic centimeter of 1:5,000 dilution of type b *H. influenzae* polysaccharide† is introduced intracutaneously.

*The organisms in the suspension used for this purpose must show good capsules. The original spinal fluid serves as an ideal suspension for this purpose if organisms are numerous and if formalin to a concentration of 0.4 per cent is added within an hour of withdrawal. Tubes of the spinal fluid after the addition of 0.4 per cent formalin are placed on ice promptly and kept there except for five minutes daily when they are taken out to remove a small specimen for use; under these circumstances the encapsulated organisms remain in good condition. If it is necessary to use a culture for this suspension, the importance of a young culture in Levinthal broth (four to six hours' incubation) must be stressed. The capsules start to degenerate after this period. In any case, one should check the condition of the capsules by known diagnostic sera before using them for detection of free antibody in the patient's serum.

†The polysaccharide was isolated by Dr. Michael Heidelberger.

The positive test, indicative of excess of anticarbohydrate antibody in the patient, is an immediate type of reaction (within five to ten minutes) which remains for approximately thirty minutes. This reaction is characterized by a wheal with extrusion of pseudopods.

TREATMENT

Meningitis.—The spontaneous mortality of this disease varies from 92 to 100 per cent when all age groups are considered. In a group of 127 patients more than 2 years of age, the death rate was found to be 80 per cent.[24] Fothergill[2] reports that with the use of horse serum and complement in 200 cases, the mortality was still 84 per cent. Treatment with horse serum and complement combined with sulfonamide therapy has produced very inconstant results, varying from 92 to 54 per cent mortality.[25, 26, 27, 28, 29] In the Boston Children's Hospital where the most extensive experience with this form of therapy has been accumulated, a recent verbal report indicated that the mortality had not been significantly influenced by the introduction of sulfonamide treatment. Instances of recovery have been reported when sulfanilamide, sulfapyridine, or sulfathiazole has been used alone. Most of the publications include one or two cases with summaries of previously reported cases. Mitchell has recently reviewed this literature.[30] Such appraisals are misleading, for it is clear that individual successes are published more frequently than repeated failures. The only paper which contains data on a significant number of patients treated exclusively by chemotherapy in one institution or vicinity is that of Aleman,[26] who reported eighteen patients treated with sulfapyridine alone with a mortality of 72 per cent. Of fifty patients treated only with sulfanilamide, gathered from the literature and from the author's experience, 88 per cent were fatal. Unless a reported series be analyzed with regard to the age of the patients, as has been so well demonstrated by Aleman,[26] and unless objective evidence on the severity of the infections be taken into consideration, it is not possible to evaluate the true efficiency of the therapy used. Neal's[29] report demonstrates the importance of the age factor. Only twenty of the twenty-nine patients were under 5 years of age and four were adults. It is worth noting that there were no recoveries in patients under 2 years of age; and when only those children under 5 years of age are considered, the mortality is 65 per cent, as contrasted with 49 per cent for all ages. Most of the patients in Neal's group were treated with sulfapyridine and horse serum.*

Insecurity of bacteriologic technique casts doubt on the identity of the organism in some of the patients with *H. influenzae* meningitis reputed to have been cured by sulfonamide alone. However, it is clear that recoveries do occur when all the commonly used sulfonamides are

*Made by New York City Health Department.

used without addition of antibody. Such evidence, supported by the demonstration of their inhibition of this organism both in vitro and in vivo, warrants the use of sulfonamide therapy for its inhibitory effect. The selection of the best drug cannot be made at the present time. Our own results in mouse protection tests and patients fail to show a significant difference among the various compounds. Sulfapyridine depresses the white blood cell count in the young group more frequently than the others. Sulfathiazole penetrates the normal blood-brain barrier with difficulty, so that the level obtained in the spinal fluid is only about one-third that of the blood. For these reasons, we have employed sulfanilamide more often than other derivatives and have felt until recently that it was the drug of choice. Sulfadiazine has been shown at least to equal sulfanilamide and sulfapyridine in its power to protect mice against lethal doses of *H. influenzae*. This fact together with its lower yield of toxic reactions suggests that sulfadiazine is the drug of choice for use in conjunction with specific antibody in the treatment of *H. influenzae* infections. Since sulfanilamide has been used in the majority of our patients, this drug is mentioned in the schedule described.

TABLE I

ROUTE OF SERUM ADMINISTRATION WITH RESULTS IN H. INFLUENZAE MENINGITIS

	TOTAL	RECOVERED	FATAL
Intravenous Only	17	16	1
Intravenous + Intrathecal	33	21	12
Totals	50	37	13

Thus far we have records of fifty patients with *H. influenzae* meningitis treated with a combination of sulfonamides and specific rabbit antiserum. In thirty-three of the fifty patients, antibody was administered both intrathecally and intravenously; in seventeen, by the intravenous route only. On the basis of our experience in this group, the latter avenue is not only justified but is considered the route of choice in all patients, except for two considerations which will be explained later. When serum was given by vein alone, the spinal fluid became sterile just as rapidly as when serum was injected intrathecally in addition (Table I). The increased meningeal irritation due to introduction of serum into the subarachnoid space was eliminated. A smooth clinical course followed, making evaluation of progress more reliable. Discomfort caused by treatment was greatly reduced. Despite these implications, intrathecal serum seems indicated in those cases in which the infection has assumed a chronic form or in acute types showing poor meningeal cellular response despite the presence of numerous organisms in stained preparations of the fresh spinal fluid.

Table I presents results of the two variations in route of therapy; namely, when antibody was used both intravenously and intrathecally

and when it was limited to the intravenous route. The high recovery rate in the group treated by the intravenous route alone is somewhat misleading, since failure to respond in forty-eight hours was followed by intrathecal serum in addition. This has been necessary only occasionally.

TABLE II

TIME REQUIRED TO STERILIZE SPINAL FLUID IN H. INFLUENZAE MENINGITIS

ROUTE OF SERUM	24 HR.	48 HR.	72 HR.	6 DAYS	23 DAYS	N.K.*
Intravenous and intrathecal	11	1	1	3	3	2
Intravenous	13	3	0	0	0	1
	24	4	1	3	3	3

*N. K. Exact period necessary not known.

In Table II the time required to sterilize the spinal fluid is listed to permit comparison of the rapidity of response under the two routes of serum administration. It is seen that the rapidity of the response in the intravenous group is quite comparable to that when intrathecal serum is used in addition.

Details of Treatment of Meningitis.—As soon as the diagnosis of type b *H. influenzae* meningitis has been established, the following treatment is carried out. A continuous intravenous infusion is set up and to patients who have received no sulfonamide previously, 0.1 Gm. per kilogram of the patient's body weight of sulfanilamide (0.8 per cent in isotonic sodium chloride) is given rapidly. During the first four hours another 0.1 Gm. per kilogram of sulfanilamide is administered along with 5 per cent dextrose in Ringer's solution (40 c.c. per kilogram) which is used in an attempt to speed up urinary excretion of the free type-specific carbohydrate of *H. influenzae.* This is advised on the premise that a given quantity of antibody would be more effective if utilized mainly against the carbohydrate in the capsule of the organism. Inhibition of the organisms by chemotherapy should prevent the further liberation of large amounts of free carbohydrate into the blood and spinal fluid. It is believed that this method of attempting to control the amount of specific carbohydrate present in the body fluids prior to serum administration is important in all cases in which no sulfonamide therapy has been used. In the early fulminating case or in cases of average severity previously untreated over a period of two to four days, the body fluids usually contain large quantities of free specific carbohydrate. In addition to its affording the most efficient use of a given amount of antibody, this procedure for speeding up excretion of free specific carbohydrate should prevent the violent reactions of the very severe forms of meningitis when a large quantity of antibody is given at one time. It is thought that such reactions result from the sudden union of large quantities of antigen and antibody. At the end of the

first four-hour period, the concentrated rabbit antibody (the dose of which will be discussed later), diluted in 10 c.c. Ringer's or saline solution per kilogram, is added to the reservoir of the continuous infusion, and the speed is adjusted so that the diluted antibody administration is completed within two hours. The infusion is then slowed so that during the next twenty hours 125 to 150 c.c. of fluid per kilogram is delivered; to this, 0.02 Gm. per kilogram of sulfanilamide is added at four-hour intervals. At the end of the first twenty-four hours of treatment, the patient has received large quantities of fluid by vein, a total of 0.3 Gm. per kilogram of sulfanilamide parenterally, and presumably enough antibody to establish an excess after neutralization of all antigen present. The recommended dose aims to provide at one time the amount of antibody necessary to accomplish this result.

Amount of Antibody.—Our experience suggests that the level of the spinal fluid sugar before treatment reflects the severity of infection. The quantitative determination of the sugar in the spinal fluid must be performed promptly after withdrawal or fluoride added as a preservative, in order to prevent decrease of sugar on standing. With this precaution, dosage of antibody is recommended in Table III.

TABLE III

SCHEDULE OF DOSAGE BASED ON SPINAL FLUID SUGAR

SPINAL FLUID SUGAR (MG. PER CENT)	MG. ANTIBODY NITROGEN INDICATED
<15	100
15 to 25	75
25 to 40	50
Over 40	25

TABLE IV

A QUALITATIVE TEST FOR ESTIMATING SUGAR IN MILLIGRAMS PER CENT IN SPINAL FLUID

TUBE NUMBER	CSF C.C.						
1	0.05	+	0	0	0	0	0
2	0.1	+	+	0	0	0	0
3	0.15	+	+	+	0	0	0
4	0.2	+	+	+	+	0	0
5	0.25	+	+	+	+	+	0
Mg. % sugar		Over 50	40 to 50	30 to 40	20 to 30	10 to 20	<10

+ = Reduction of Benedict's Solution.
0 = No reduction of Benedict's Solution.

When patients are admitted during the night, a qualitative test which provides an estimate of the quantity of sugar is very useful. One cubic centimeter of Benedict's solution is added to each of five tubes (dimensions 75 mm. × 12 mm.). The quantity of spinal fluid added to each tube is indicated in Table IV; also, the sugar values in milligrams per

cent, depending upon the tubes showing reduction, are listed. Such an index is intended only as a preliminary guide. When the sugar values suggest that the severity is on the border line between two groups, the next smaller amount of antibody nitrogen may be used. Table V demonstrates the prognostic value of the spinal fluid sugar. In thirty recovered patients whose spinal fluid sugar was measured before treatment, only two showed levels less than 15 mg. per cent. By contrast, in the group of ten fatal cases in which this determination was made, eight were in the range below 15 mg. per cent. The patient of the recovered group with a level of less than 10 mg. per cent had a fulminating type of the disease but was admitted promptly, after only twenty-four hours' illness.

TABLE V

PROGNOSTIC VALUE OF THE QUANTITATIVE SUGAR ON THE ORIGINAL SPINAL FLUID IN H. INFLUENZAE MENINGITIS

	SPINAL FLUID SUGAR LEVELS; MILLIGRAMS PER 100 C.C.						
	N.D.*	<10	10-15	15-20	20-30	30-40	>40
Recovered Group	7	1	1	3	8	8	9
Fatal Group	3	6	2	1	1	0	0

*No original determination.
< Less than; > greater than.

Studies of other laboratory procedures for appraising the severity of infection are in progress. Precipitin tests on the spinal fluid, serum, and urine suggest that valuable evidence will be obtained by these methods, but at present information is too limited for use as a guide to treatment.

One hour after the administration of the dose considered on the basis of the laboratory examination to be sufficient for recovery, the temporary adequacy of treatment is tested by examining the patient's serum for its ability to produce capsular swelling of a suitable suspension of *H. influenzae*. This procedure, described under the section on Tests Useful in Therapeutic Program, must be repeated daily for at least the first week, since it seems to be important to have an excess of free antibody until it is certain that the infection has been overcome. When excess antibody is not demonstrable by the method described, an additional dose equivalent to 25 mg. of antibody nitrogen is given and the serum retested one hour later. A good degree of correlation between the results of capsular swelling capacity of the patient's serum and the polysaccharide skin test has been found. However, our experience with the latter is inadequate to recommend it as the sole method for appraising antibody excess.

In following the progress of our patients, we have been guided to a large extent by the changes developing in the spinal fluid, which for a

time we examine daily. If within twenty-four hours the spinal fluid sugar and chlorides have risen, the cell count has decreased, no organisms are seen on direct smear, and the patient's serum causes capsular swelling when diluted 1:10, no further antibody is needed provided all these elements continue to progress toward their normal level, the cultures become and remain sterile, and antibody remains present in excess. In all relatively early infections it has been our policy to limit serum administration to the intravenous route for a period of forty-eight hours after the institution of antibody therapy. If at the end of this period evidence of satisfactory progress is lacking, a volume of serum (approximately 5 c.c.) equivalent to 25 mg. of antibody nitrogen is administered intrathecally.

After sulfanilamide has been given parenterally for twenty-four hours and the patient appears better, 0.1 Gm. per kilogram is administered daily by mouth, divided in six doses at four-hour intervals, and is continued for seven days after the spinal fluid is first shown to be sterile.

TABLE VI

RESULTS OF COMBINING RABBIT ANTIBODY AND CHEMOTHERAPY IN H. INFLUENZAE MENINGITIS

SUMMARY OF RESULTS BY YEARS			
YEAR	NUMBER RECOVERED	NUMBER FATAL	TOTAL
1938-1939	8 (57%)	6 (43%)	14
1940	15 (75%)	5 (25%)	20
1941	14 (88%)	2 (12%)	16
Totals	37 (74%)	13 (26%)	50

The program of treatment is effective. Table VI summarizes our therapeutic results by years. During the 1938-1939 period the patients were treated with unconcentrated rabbit serum made at the Babies Hospital. Squibb's concentrated antibody solution, produced and tested according to our specifications, was used for all other patients. We are indebted to the New Haven Hospital for the results of treatment of fourteen of these cases. The evidence indicates that the improvement in results over this four-year period is due chiefly to a more efficient application of the quantitative approach. It has not been due to a more favorable age distribution of patients. Judged by our present criteria, in three of the six fatal cases of 1939 treatment was inadequate.

Table VII presents the significant data on the thirteen fatal cases. As we view the matter at the present time, the first three patients were not treated adequately. The fourth patient, after apparently complete recovery for sixteen days, continued to show leucopenia after withdrawal of sulfapyridine. Meningitis recurred, this time in a fulminating form which failed to respond to therapy. At autopsy, signs of both healed and fresh meningitis were evident. The fifth patient was im-

proving and the spinal fluid had been sterile for three days when leucopenia made its appearance; after forty-eight hours she died. Since the beginning of 1940, with two exceptions (B. V. and M. F.), the fatalities

TABLE VII

ANALYSIS OF FAILURES IN THE TREATMENT OF H. INFLUENZAE MENINGITIS

NAME	AGE	DRUG	ANTIBODY (TOTAL MG.)	BLOOD CULTURE	TIME TO STERILIZE SPINAL FLUID	SPINAL FLUID SUGAR (MG. %)
			1939			
J. W.	2¾ yr.	S	50	+	Not sterile	13
B. H.	1½ yr.	S	20	+	Not sterile	N. D.
J. T.	2½ yr.	S	90 + H.S.	+	Not sterile	N. D.
J. G.	2¼ yr.	P	133	0+	24 hr. for 16 days	31, 5
D. S.	7 mo.	P	300	++	24 hr. for 3 days	3
W. G.	7 yr.	P	235	+-+	72 hr. for 4 days	6
			1940			
G. F.	3 mo.	P 2 days T 16 days	175	+-+	72 hr. for 6 days	N. D.
M. W.	3 mo.	S 4 days T 19 days	180	+-+	48 hr. for 1 day	0
B. A.	4 mo.	S	75	+	Not sterile	22
D. F.	7 mo.	S 19 days	250	+	Not sterile	6
B. V.	5 yr.	P	127 + H.S.	0	48 hr. for 9 days	N. D.
			1941			
M. F.	2 yr.	S	100	0	Not sterile	<20
J. G.	6 mo.	S 2 days	100	+	Not sterile	8

S, Sulfanilamide; P, sulfapyridine; T, sulfathiazole; N.D., no original determination; H.S., horse serum.

TABLE VIII

AGE DISTRIBUTION IN RECOVERED AND FATAL GROUPS OF H. INFLUENZAE MENINGITIS

AGE	TOTAL NUMBER	RECOVERED	FATAL	PER CENT RECOVERY
3 to 7 months	8	2	6	25
7 to 12 months	3	3	0	100
1 to 2 years	14	13	1	92
2 to 3 years	18	13	5*	72
3 to 4 years	1	1	0	100
4 to 5 years	5	5	0	100
Over 5 years	1	0	1	0
Totals	50	37	13	83% recovery of patients over 7 months of age

*Two cases, leucopenia; two cases, insufficiently treated; one patient, M. F. in Table VII, has been commented on.

have been limited to infants under 7 months of age. B. V., spinal fluid was sterile for nine days when leucopenia occurred. M. F., after twelve days of treatment with sulfapyridine, manifested hemiplegia. The course of illness was merely prolonged by the addition of rabbit serum. At autopsy there was thrombophlebitis with encephalitis over the left parietal and both frontal areas.

Table VIII shows the incidence with relation to age and the results of therapy in the different age groups. It demonstrates what has been emphasized previously, that the unsatisfactory therapeutic result obtained with infants under 7 months of age constitutes our greatest problem. All evidence indicates that the high mortality in infants under 7 months of age is due to the advanced character of the disease at the time signs diagnostic of meningitis become manifest. For improvement in results at this age, we must depend upon improved clinical perception.

Table IX presents the significant data for a group of patients who received rabbit antibody and sulfonamide after prolonged periods of unsuccessful treatment by chemotherapy alone or combined with horse serum. With two exceptions, the period of previous treatment was three to four weeks. The recovery of seven of these ten patients after treatment with rabbit antibody allows two conclusions:

1. All the sulfonamide derivatives used thus far exert a significant inhibitory effect on *H. influenzae* infections in children.

2. Type-specific antibody is an essential part of therapy in a number of patients (the proportion is not yet known) with *H. influenzae* meningitis.

We have seen recurrence of infection after the original sterilization of the spinal fluid only when persistent leucopenia develops and in instances where the meningitis had assumed a chronic form before rabbit serum was used. However, all patients are kept in the hospital for one week after signs of recovery have appeared. Lumbar puncture is performed daily; this precaution is discontinued only when the chemical and cellular aspects of the spinal fluid have returned to normal and the patient remains free of fever. After this state of apparent recovery has materialized, we have seen several patients who showed a return of fever and increase of spinal fluid cells and protein. The spinal fluid cultures were sterile and the concentration of sugar and chlorides remained normal. Evidence of serum sickness, in some instances quite meager, accompanied this change in the spinal fluid. Although at the onset of this situation it is impossible to recognize the cause before the results of culture are known, our experience includes a number of patients who continued to show sterile spinal fluid and whose spinal fluid cells and protein all returned to normal in a few days. It is believed that these episodes represent localized serum reactions of the meninges. They are presumably akin to similar responses seen in patients with pneumonia who after serum treatment show sterile pleural effusions in concurrence with evidence of serum sickness elsewhere in the body. We believe that additional rabbit serum should be resorted to only when organisms are again identified directly in the spinal fluid or in cultures by the capsular swelling method described previously. Resumption of chemotherapy is justified under these circumstances.

TABLE IX

PATIENTS TREATED IN OTHER HOSPITALS WITH OTHER FORMS OF THERAPY FOR LONG PERIODS PRIOR TO THE USE OF TYPE B RABBIT ANTIBODY

NAME	AGE	DURATION OF ILLNESS	PREVIOUS THERAPY	BLOOD CULTURE	SPINAL FLUID				ANTIBODY MG. IMMUNE N	RESULT
					SUGAR (MG. %)	CHLORIDES (MG. %)	TIME TO STERILIZE	SMEAR		
R. Z.	5 yr.	17 days	P, 17 days	0	N.D.	N.D.	24 hr.	0	100	Recovered
E. A.	14 mo.	13 days	P, 11 days	+	22	666	3-6 days	+	200	Recovered
H. W.	22 mo.	30 days	N + P + T, 4 wk.	N.D.	N.D.	N.D.	3 days	+	100	Recovered
W. H.	2 yr.	21 days	P, 20 days	N.D.	37	688	24 hr.	0	100	Recovered
M. M.	3 yr.	20 days	P + D + H.S., 19 days	+, 0	36	691	48 hr.	+	100	Recovered
B. G.	9 mo.	38 days	T + P + H.S.	0	30	N.D.	48 hr. 23 days	+	175	Recovered
R. G.	3 yr.	4 wk.	P + H.S., 4 wk.	0	18	590	5 days	+	150	Recovered
J. S.	2 yr.	8 days	P, 8 days	0	31-5	621	24 hr. 16 days	+	130	Died
J. Sh.	3 yr.	4 wk.	P + H.S., 3 wk.	0	7	604	N.S.	4+	100	Died
M. F.	2 yr.	12 days	P, 12 days	0	25	N.D.	N.S.	4+	100	Died

P, Sulfapyridine; T, sulfathiazole; N.D., no determination; N, neoprontosil; D, sulfadiazine; N.S., not sterilized; H.S., horse serum.

Duration of illness column presents time between onset of meningitis and the institution of rabbit antibody.

Blood culture and spinal fluid chemistry results refer to those examinations made just before rabbit antibody was administered.

In patients B. G. and J. S., under the column "Time to Sterilize Spinal Fluid," the second time element listed indicates the number of days following the first antibody administration when a recurrence of meningeal infection supervened. In the first instance the recrudescence was only a temporary one, which responded to additional antibody treatment.

TREATMENT OF INFECTIONS WHICH PRODUCE OBSTRUCTION OF THE RESPIRATORY TRACT

In these critically ill patients one is faced with two problems: relief of obstruction to respiration and treatment of the local infection and bacteremia.

Tracheotomy is frequently imperative within a few hours after onset of dyspnea. In other patients, when this procedure is not obviously urgent, exact criteria for intervention are controversial even among those with most experience. Sudden complete obstruction, following manipulation within or outside of the respiratory tract, is seen not infrequently. For this reason the Mosher life saver is a necessary part of the equipment for handling these patients prior to tracheotomy. Only three patients, 15 per cent of the combined series presented in Table X, recovered without tracheotomy. One of these patients was 11 years old. Since the probability of the need for tracheotomy is so great and the risk of delaying too long is so hazardous, early operation, while circumstances are still favorable, is strongly advised.

TABLE X

RESULTS OF TREATMENT USED AT THE BABIES HOSPITAL AND NEW HAVEN HOSPITAL IN H. INFLUENZAE INFECTIONS CAUSING OBSTRUCTION OF THE RESPIRATORY TRACT

TREATMENT USED	RESULTS		
	RECOVERED	FATAL	TOTAL
Tracheotomy; no specific therapy	1	3	4
Tracheotomy + sulfonamide	6	0	6
Tracheotomy + sulfonamide + serum	4	0	4
Sulfonamide + serum; no tracheotomy	1	0	1
Sulfonamides only; no tracheotomy	2*	0	2
No treatment	0	3	3
	14 = 70%	6 = 30%	20

*Ages of two patients were 11 years and 6 years.

Rapid identification of the causative organism and determination of the severity of the infection are essential for effective therapy. Strong presumptive evidence of the responsible agent is obtained when direct examination of nasopharyngeal mucus reveals the presence of type b *H. influenzae* by the capsular swelling method.[20] Further confirmation is obtained when the mucus from the trachea, after tracheotomy, is shown to harbor the same organisms. In many cases the ultimate proof must await demonstration of bacteremia. However, in the most severe infections the final proof of etiology, as well as an immediate index of severity, may be contributed by demonstrating the presence of type-specific carbohydrate in the patient's serum, using the precipitin test described.

The same treatment, tracheotomy and sulfonamide therapy, is indicated during the first four-hour period for all patients with this form

of *H. influenzae* infection. When a patient with evidence of acute obstruction of the respiratory tract is admitted, a Mosher life saver[31] and tracheotomy set should be in the room before the physical examination is attempted. Equipment for taking nasopharyngeal, throat, and blood cultures and for collecting a small specimen of blood for serum should be at the bedside in order to eliminate all unnecessary disturbance later. Immediately following the physical examination and collection of the specimens indicated, an infusion of sulfanilamide (0.1 Gm. per kilogram) in saline is given and a continuous intravenous infusion set up. Subsequent chemotherapy over the first twenty-four hours follows the schedule described under the section on Meningitis. During this four-hour period of continuous intravenous chemotherapy, the mucus from the nasopharynx and material from the trachea are examined directly by the capsular swelling method. The patient's serum is examined for evidence of specific-soluble substance by the precipitin test, and if found negative after a thirty-minute period, a carbohydrate skin test is performed.

Since some of these patients respond promptly to sulfonamides alone, the essential problem at present is to select those to whom administration of antibody in addition is probably essential for recovery. Examination of the blood and urine for a crude estimation of the amount of type-specific carbohydrate present in the body fluids is of value in gauging severity. It is our custom to use antibody in addition to sulfonamides in those patients whose serums show a positive precipitin test within a ten-minute period after the test is set up, for it is believed that they represent the severest cases. When it is not possible to demonstrate even a trace of type-specific carbohydrate in the patient's serum, the carbohydrate skin test may be used in detecting evidence of type-specific antibody in the manner described under the section on Tests Useful in Therapeutic Program. It is believed that those patients who show evidence of antibody production represent the mildest form of the infection. We have failed to demonstrate antibody prior to treatment in the three patients tested. This is to be expected since all of our patients, as well as those of Sinclair[6] in New Haven, have had bacteremia. The interval which elapses between the onset of blood stream invasion and hospital admission is not sufficient for production of antibody. At least a few days of inhibition of bacterial growth by chemotherapy are probably required before the host is able to manufacture an amount of antibody sufficient for demonstration by the methods used.

In patients who show a positive precipitin test within ten minutes it is our custom to give an amount of type b *H. influenzae* rabbit serum (approximately 10 c.c.) which contains 50 mg. of antibody nitrogen. The concentrated serum, diluted with 10 c.c. of Ringer's solution per kilogram of body weight, is added to the continuous infusion after the first four-hour period during which sulfanilamide and fluids have been

administered. The adequacy of the dose is checked by examining the patient's serum for excess of free antibody by the capsular swelling method. If the patient shows extension of the inflammatory process into the finer bronchi, as evidenced by failure of tracheotomy to relieve the respiratory obstruction, we believe that antibody should be used, even though results of precipitin test fail to furnish the criterion which we have established for ourselves as the indication for use of antibody, when the serum fails to show evidence of large amounts of specific soluble substance in the body fluids. The need for antibody therapy in all other cases showing a negative test for specific-soluble substance must be judged by the patient's response to sulfonamides over a twenty-four-hour period. Of the three patients who have been admitted to the Babies Hospital since the institution of this schedule of treatment, only one showed evidence of large quantities of type-specific carbohydrate in the serum. This patient was treated with antiserum according to the plan described, and the response was prompt. The other two, because the precipitin tests were negative, were given a trial of sulfanilamide by continuous intravenous infusion. One of them showed no response of temperature or general condition over a twenty-four-hour period. Rabbit antiserum was then given with significant improvement within less than twenty-four hours. In the most recently treated patient, sulfanilamide was used for forty-eight hours with slight improvement. During the third day, however, the temperature rose again and the child remained drowsy and sick. Following the administration of antibody, the patient improved rapidly. In the three patients who recovered following sulfonamides and tracheotomy, the temperature response was as rapid as it has been in three patients following the use of type b antibody in addition, but we have no data on polysaccharide tests in any of these patients.

Analysis of results of treatment at the Babies Hospital and those of the New Haven Hospital, the latter published by Sinclair,[6] is shown in Table X. The effectiveness of sulfonamides combined with tracheotomy but without rabbit antibody is striking and warrants a trial in all but the most severe cases selected by the method described.

Table XI presents the relevant data on our ten cases of type b *H. influenzae* infections causing obstruction of the respiratory tract. It demonstrates the uniformity of the history and clinical features. All the patients were over 2 years of age. The onset of any indication of illness occurred less than twenty-four hours before admission, except in the case of the 11-year-old boy, who had fever and sore throat for forty-eight hours. Dyspnea became severe so rapidly that all patients, except the one cited, were admitted to the hospital within a few hours of onset. Epiglottitis was a constant feature. In only one of the patients who recovered was the inflammatory process found to extend into the trachea and bronchi. In patient M. F. empyema developed early in spite of

TABLE XI

SIGNIFICANT DATA ON THE PATIENTS SHOWING OBSTRUCTIVE LESIONS OF RESPIRATORY TRACT DUE TO H. INFLUENZAE

NAME	AGE	DURATION OF SYMPTOMS		PATHOLOGY		BLOOD CULTURE	TREATMENT			RESULTS
		FEVER AND SORE THROAT	DYSPNEA	EPIGLOTTITIS	OTHER TYPES		DRUG	RABBIT SERUM	TRACHEOTOMY	
R. M.	2 yr.	4 hr.	4 hr.	+	0	+	S	+	+	Recovered
G. W.	4 yr.	12 hr.	6 hr.	+	0	+	S	+	+	Recovered
F. J.	4 yr.	24 hr.	3 hr.	+	Pneumonia; adenitis	+	S	+	+	Recovered
S. S.	8 yr.	12 hr.	5 hr.	+	0	+	P	0	+	Recovered
R. R.	11 yr.	48 hr.	24 hr.	+	0	+	S	0	0	Recovered
M. F.	5 yr.	†	3 hr.	+	L.T.B.; empyema	+	S + P	0	+	Recovered
							Surgical drainage			
F. O.	4 yr.	14 hr.	3 hr.	+	0	+	S	0	+	Recovered
A. C.	2 yr.	18 hr.	2 hr.	+	Periarticular abscess	+	0	0	+	Recovered
							Surgical drainage			
E. L.	2 yr.	12 hr.	6 hr.	+	L.T.B.; pneumonia	+	0	0	+	Died 2 hr.
E. H.	4 yr.	18 hr.	12 hr.	±*	Pharyngeal cellulitis	+	0	0	0	Died 2 hr.

*No examination of larynx or epiglottis was made but child breathed in a manner characteristic of supraglottic stenosis.
S, Sulfanilamide; P, sulfapyridine; L.T.B., laryngotracheobronchitis.

sulfonamides, and the bacteremia continued over a three-week period. After a febrile course of five weeks, she finally recovered following rib resection. One of the patients who died was shown to have extension of the process throughout the bronchial tree and pneumonia in addition. The other was not examined post mortem.

PNEUMONIA AND EMPYEMA WITH BACTEREMIA IN INFANTS UNDER ONE YEAR OF AGE

The unfavorable outlook for infants with this variant of the infection justifies the use of type-specific antibody as soon as empyema with bacteremia due to type b *H. influenzae* is recognized. By the time these infants reach the hospital the empyema is usually well established and the organisms may be identified directly from the fluid. In other instances the positive blood culture gives the first lead to the etiology, the baby having been treated for pneumonia with sulfonamides without response.

Because of the frequent development of meningitis following bacteremia and the difficulty experienced in recognizing its presence in young infants, we have adopted the policy of performing lumbar puncture in all such cases. If meningitis is shown to be present, it is treated in the manner already described. If the meninges are not yet involved, antibody equivalent to 50 mg. of antibody nitrogen is given initially and its sufficiency checked within one hour. Aspiration of pleural fluid is practiced when necessary to relieve respiratory embarrassment. We have seen a 10-month-old infant with empyema, meningitis, and bacteremia recover following the use of sulfonamides and specific antibody.

DISCUSSION

The great variation in the severity of *H. influenzae* infections is only partially understood; an effort will be made to summarize what is known. In contrast with the severe infections already described, mild examples are also seen which assume the form of paranasal sinusitis or pneumonia in children over 2 years of age. Even the bacteremias, both those which not infrequently follow benign infections and those which are a constant component of the more severe infections, differ greatly in their evolution. In children over 3 years of age the blood stream may become sterile spontaneously or after chemotherapy without producing localized lesions. At times suppurative arthritis or subcutaneous and deep abscesses occur; rarely the organisms locate on the heart valves. Peritonitis is seldom seen except in patients who have edema, as in nephrosis and lupus erythematosus, and then it is an infrequent complication. Meningitis is the most frequent and serious complication of bacteremia.

Susceptibility to invasion of the blood stream is believed to be due to a lack of immunity of the infant or child, in contrast to the adult, who is relatively resistant to this organism. Fothergill and Wright,[32] by

making determinations of the bactericidal properties of the blood of normal children and adults against the mucoid phase of type b strains, found suggestive evidence on this point. They showed that at all ages there is an inverse relationship between the incidence of meningitis and the bactericidal properties of the blood. Although its character has not been studied, this power of the blood is believed to be due to antibody. The difference in the bactericidal property of the blood at the same age period is conjecturally responsible for the variation in severity, even in similar age groups.

If the assumption be correct that type-specific antibody is an essential part of the recovery mechanism, it should be possible to demonstrate antibody production in those patients who recover under sulfonamide without complementary serum therapy. Our own experience includes evidence of complete recovery of one patient with type b *H. influenzae* meningitis with sulfanilamide alone. The child was 3 years of age. She had been treated for five days with sulfanilamide for a relatively mild infection. Although meningitis was present, the child looked well and was able to sit up in bed. The spinal fluid contained 900 cells per cubic millimeter, but no organisms were seen in stained smears and the sugar and chloride were normal. After three days' incubation, the original spinal fluid grew type b *H. influenzae*. By this time the child's general condition, temperature, and spinal fluid showed striking improvement; her serum agglutinated a suspension of encapsulated *H. influenzae*. Under these circumstances serum administration seemed unnecessary, a judgment which proved to be well founded, for the child recovered. It is hoped that such evidence along with polysaccharide skin tests[23] for detecting antibody may prove of value in separating the patients who require added antibody for recovery from those who have formed sufficient immune substance as a result of a mild infection which has been efficiently suppressed by chemotherapy early in the course.

Factors other than antibody, the production of which is so closely correlated with age, obviously play a part. Investigation of virulence of strains isolated from fatal and recovered cases has failed to demonstrate a significant difference. However, the method employed is identical with that used for assessing the virulence of meningococci;[33] it tests the virulence for mice only. Prolongation of infection at the time treatment is started plays a very important role in these syndromes and determines to a great extent the response to sulfonamide alone or combined with specific antibody. On the other hand, the onset may be sudden after an apparently innocuous upper respiratory infection, and the disease may pursue an explosive course from the beginning. One can only speculate about the factors which influence the initial severity. The size of dose of infecting agent, though conceivably an important consideration, is impossible to evaluate. At times a preceding virus infection may be a significant factor in host resistance. In chimpanzees, Dochez

and associates[34] have observed that during infections with the virus of the common cold the nontypable or relatively innocuous *H. influenzae* which the animals habitually carry in the respiratory tract may be replaced by the typable, mucoid, or potentially pathogenic strains.

Under the influence of chemotherapy alone, an infection of the meninges of average severity may be held in a static phase for a long period, provided there is no interruption of treatment and provided adequate levels are maintained. If the infection is mild from the beginning and sulfonamides are started early, the natural antibody formed by the host in response to the infection is sufficient for complete recovery.

Limited experience suggests that when free antibody has been shown to be present by the methods suggested, the outcome may be expected to be favorable with sulfonamide alone and that type-specific antibody may be reserved. However, many institutions and most private practitioners lack facilities for demonstrating free antibody. Moreover, the techniques now available are still in the experimental phase. Accordingly, it is advocated that all patients suffering from meningitis and obstructive infections of the respiratory tract and infants under 1 year of age with empyema and bacteremia receive type-specific rabbit antibody in addition to sulfonamide.

SUMMARY

The clinical features of the following infections with type B *H. influenzae* are presented: meningitis, respiratory infection causing obstruction of the respiratory tract, and pneumonia complicated by empyema in infants under 1 year of age. A therapeutic program is outlined for each of these groups.

The biology of *H. influenzae* is discussed for purposes of clarifying the principles which have been applied in treatment. Laboratory tests useful in the therapeutic program are presented.

The results of the treatment advised in meningitis are analyzed from several points of view. Of the fifty patients reported, thirty-seven, or 74 per cent, recovered.

The treatment of ten patients with obstructive infections of the respiratory tract is discussed.

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OBSERVATIONS ON HEMOPHILUS INFLUENZAE (TYPE B) MENINGITIS OF CHILDREN

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THE advent of chemotherapy and serotherapy has radically changed the outlook of *H. influenzae* meningitis. Until a few years ago, the mortality rate of this disease was exceedingly high, and recoveries occurred in less than 5 per cent of all cases, irrespective of the various measures taken, such as repeated spinal taps and forced spinal drainage. Today, two specific agents are available for the treatment of this disease; namely, type-specific antibodies and sulfamido compounds. It is of paramount importance to diagnose this condition early and to start specific treatment as soon as possible.

In this communication, observations on 62 cases of *H. influenzae* meningitis of children are reported. Special attention has been given to the following: (1) bacteriologic and immunologic diagnosis; (2) incidence of bacteremia; (3) effect of treatment with type-specific anti-*H. influenzae* serum obtained from horse and rabbit, and with the various sulfamido compounds on the spinal fluid and the outcome of the disease; (4) the relationship between demonstrable antibodies in the blood and the presence of viable *H. influenzae* or specific-soluble substance in the spinal fluid of these patients.

The Bacteriologic and Immunologic Diagnosis of H. Influenzae Meningitis.—The bacteriologic and immunologic diagnosis of typical cases of *H. influenzae* meningitis presents no difficulties. Usually, the spinal fluid contains many leucocytes and pleomorphic, slender, gram-negative bacilli, often coccoid forms. The organisms grow on blood and chocolate agar, particularly in an atmosphere of 10 per cent carbon dioxide, and fail to grow on plain agar, in plain broth, or on Endo agar. It should be pointed out, however, that in a few instances profuse growth of *H. influenzae* was obtained from spinal fluid using plain infusion broth without the addition of blood, hemoglobin, or like substances. It is probable that some of the growth factors were present in the spinal fluid used for seeding purposes, since subcultures to broth failed to grow out. Only in rare instances are gram-negative bacilli other than *H. influenzae* (such as Friedländer's bacillus, *B. proteus, B. pyocyaneous,* members of the *B. coli* group, typhoid and paratyphoid bacilli) the cause of purulent meningitis. These organisms grow readily on Endo agar in contradistinction to *H. influenzae.*

Sometimes *H. influenzae* grows in the spinal fluid itself following incubation at 37° C. for one to four days. The increase in the number

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of this organism, however, is by no means as striking as in the case of the meningococcus. The latter organism usually grows profusely in the spinal fluid of patients with meningococcal meningitis.

Two methods are available to determine within a few hours the nature of the infecting gram-negative organism present in the spinal fluid. In the first place, a capsular swelling (Quellung) may be obtained by the addition of anti-*H. influenzae* rabbit serum. In the second place, the specific-soluble substance of *H. influenzae* can be demonstrated in the supernatant of the spinal fluid. This precipitation test is also recommended by Lindsay, Rice, and Selinger,[1] by Finland and Dingle,[2] and others. The following technique has been employed: The spinal fluid is centrifuged and the clear supernatant is mixed with equal amounts of anti-*H. influenzae* serum. It is important to point out that undiluted serum may fail to cause precipitation, whereas serum in a dilution of 1:10 may do so. For this reason, various serum dilutions (1:1, 1:10, and 1:100) are used. Usually, with suitable amounts of serum, precipitation occurs within a few minutes. Otherwise, the mixtures are incubated at 37° C. for several hours. As controls, the supernatant of the spinal fluid without serum and mixed with meningococcal or other serums is used.

A positive Quellung or precipitation test with suitable type-specific serum not only proves that the causative agent is *H. influenzae,* but also that the organism belongs to type b. This type is by far the most common type in *H. influenzae* meningitis. At the Children's Hospital, no other type of this organism has as yet been found in this condition.

Occasionally, spinal fluid from patients with *H. influenzae* meningitis, particularly in the early stage, may reveal but few leucocytes and microorganisms or no bacteria at all, even when the sediment of the spinal fluid has been carefully examined. In these instances, both the capsular swelling and precipitation tests may be negative, and it may be necessary to defer the diagnosis until the culture has been completed. It has been observed on several occasions that spinal fluid taken twelve to twenty-four hours later may reveal a marked increase in the number of leucocytes and bacteria. It is advisable, therefore, to perform a second spinal tap after a lapse of twelve to twenty-four hours in these cases in which meningitis is suspected clinically. This seems to be particularly indicated during epidemics of poliomyelitis and other diseases of the central nervous system. An illustrative case ensues. B. O., a patient of Dr. Douglas P. Arnold, was admitted to the Children's Hospital with signs of meningeal irritation. This occurred in the summer of 1939 during a severe outbreak of poliomyelitis in this area. The spinal fluid contained 12 leucocytes per cubic millimeter; the Pandy test was negative; no organisms were seen on film, and the culture was sterile. Twenty-four hours later the spinal fluid contained 6,280 leucocytes per cubic millimeter; the Pandy test was positive, and *H. influenzae* was found on culture.

Incidence of Bacteremia in H. Influenzae Meningitis of Children.—The incidence of bacteremia in patients with *H. influenzae* meningitis is relatively high. As shown in Table I, *H. influenzae* was recovered from the blood of 11 out of 17 cases. A high incidence of bacteremia in this condition was also reported by Alexander[3] who found 17 bacteremic cases in a series of 25 patients with *H. influenzae* meningitis. Neal, Jackson, and Appelbaum[4] recovered *H. influenzae* from 7 out of 8 patients; Rivers[5] in 8 out of 18 cases, and Hart[6] in 4 out of 7 instances. It seems advisable, therefore, to culture the blood in all cases of *H. influenzae* meningitis. Moreover, the finding of such a high incidence of bacteremic cases may point to a hematogenous origin of the meningitis in these cases.

TABLE I

H. INFLUENZAE MENINGITIS

CASE	AGE	BLOOD CULTURE (H. INFLUENZAE)	TREATMENT	DURATION OF HOSPITALIZATION	OUTCOME
M. S.	3 yr., 5 mo.	----	Sp	24 hours	Died
A. S.	11 mo.	----	S, Sp	17 days	Died
N. S.	18 mo.	Negative	Sth	15 days	Recovered
P. F.	3 yr., 5 mo.	Negative	HS, S, Sp, Sth	50 days	Died
J. F.	1 yr.	Positive	HS, Sp	4 days	Died
W. B.	18 mo.	----	HS, S, Sp	29 days	Recovered
M. L.	2 yr.	----	HS, Sp	3 days	Died
B. B.	8 yr.	Negative	HS, S, Sp	16 days	Recovered
M. R.	6 mo.	Positive	HS, Sp	7 days	Died
R. M.	4 yr.	Negative	HS, S, Sth	7 days	Died
B. O.	4 yr.	Negative	HS, Sp	13 days	Died
S. O.	6 yr.	Positive	HS, Sp	31 days	Died
D. N.	8 mo.	Positive	HS, Sp, Sd	20 days	Died
J. M.	6 mo.	Positive	HS, S, Sp	2 days	Died
T. C.	15 mo.	Positive	HS, S, Sth	44 days	Died
L. B.	19 mo.	----	RS, S, Sp, Sd	28 days	Died
J. R.	3 yr., 5 mo.	----	RS, S	2 days	Died
M. G.	2 yr.	Positive	RS, S	17 days	Recovered
R. F.	13 mo.	Positive	RS, S	7 days	Died
W. C.	19 mo.	Positive	RS, S, Sd	34 days	Recovered
R. W.	3 yr., 6 mo.	Negative	RS, S, Sp, Sd		Recovered
M. W.	3 yr., 6 mo.	Positive	RS, S, Sp, Sth	25 days	Recovered
C. A.	7 yr.	----	----	Less than 24 hours	Died
R. B.	8 mo.	----	----	24 hours	Died
M. D.	10 mo.	Positive	----	Less than 24 hours	Died

RS, Rabbit anti-*H. influenzae* serum; HS, horse anti-*H. influenzae* serum; S, sulfanilamide; Sp, sulfapyridine; Sth, sulfathiazole; Sd, sulfadiazine.

Pathogenesis of H. Influenzae Meningitis.—The primary focus of the infection cannot always be determined. An acute upper respiratory infection may precede the meningitis. In our series, *H. influenzae* was recovered from the throat or bronchi in 4 cases. It is interesting to note that in 2 patients acute laryngotracheobronchitis necessitated tracheotomy. In other cases, otitis media is found in patients with *H. influenzae* meningitis. In 3 cases of this series, *H. influenzae* was recovered from the middle ear. In rare instances *H. influenzae* septicemia may precede for days or even weeks the development of meningitis. One such case was encountered. *H. influenzae* was recovered

from the blood and from metastatic purulent lesions of several joints. Three weeks later, this patient developed *H. influenzae* meningitis and died.

In view of the high incidence of bacteremia, the possibility must be considered that these apparent primary foci could be the result rather than the source of the blood stream infection, and furthermore, that the organisms present in these foci may belong to other types than those responsible for the meningitis.

It seems possible that other microorganisms that cause an acute infection of the upper respiratory tract may enable *H. influenzae* to invade the blood stream from this lesion and thus produce meningitis. In one particular instance, severe laryngotracheobronchitis, which necessitated tracheotomy, was apparently caused by beta hemolytic streptococcus, which was recovered from the lesion in almost pure culture. Shortly afterward, this patient developed *H. influenzae* meningitis.

The Effects of Serotherapy and Chemotherapy Upon the Outcome of H. Influenzae Meningitis.—From 1927 to 1937, thirty-seven patients suffering from *H. influenzae* meningitis were admitted to the Children's Hospital. All died. From 1938 to January, 1942, twenty-five patients with *H. influenzae* meningitis were admitted. It cannot be stated definitely whether or not this points to an actual increase in the incidence of *H. influenzae* meningitis in recent years.

The results obtained in the treatment of twenty-five patients with *H. influenzae* meningitis by means of chemotherapy and serotherapy are summarized in Table I.

Three patients were treated by means of chemotherapy exclusively. One received sulfapyridine and one sulfanilamide and sulfapyridine; both died. The third, N. S., a patient of Dr. Douglas P. Arnold, was given sulfathiazole exclusively and made a complete recovery. No determinations of the concentration of the drug in the spinal fluid were carried out. This patient was treated at a time when it was not known that sulfathiazole does not pass readily into the spinal fluid. However, the possibility cannot be discarded that sulfathiazole may have some, as yet not thoroughly understood, effect in meningitis, even when present in the spinal fluid in low concentrations only.

Twelve patients received anti-*H. influenzae* horse serum in conjunction with sulfamido compounds. The serum was obtained from the Massachusetts Commonwealth through the courtesy of Dr. L. Fothergill, of Harvard University Medical School. Only 2 of these patients recovered. One of these patients who was treated with very large doses of sulfapyridine in conjunction with anti-*H. influenzae* serum was reported in detail by Jacobsen and Neter.[7] It should be pointed out that treatment with this serum in the majority of cases resulted in transitory clinical improvement paralleled by corresponding changes in the spinal fluid. This improvement, however, should not lead to undue optimism; relapses do occur.

Three patients succumbed within twenty-four hours following admission to the Hospital.

The remaining seven cases of *H. influenzae* meningitis received both type-specific anti-*H. influenzae* rabbit serum and sulfamido compounds. Four of these patients made a complete recovery.

It is interesting to note that one of the patients (R. W.) recovered from two attacks of *H. influenzae* meningitis following administration of anti-*H. influenzae* rabbit serum and sulfamido compounds. He was treated in July, 1941, and discharged on August 21, 1941, apparently cured. On October 8, 1941, he was readmitted to the hospital with purulent meningitis caused by *H. influenzae*. Again, with this specific therapy he recovered. It cannot be stated with certainty whether the second attack represented a recrudescence of the disease or a new infection. It is probable, however, that the second attack started from a latent focus of infection when protective antibodies were no longer present.

Although this series is too small for final conclusions, the results seem to indicate that at the present time Alexander's type-specific rabbit serum with chemotherapy is the most efficient treatment.

Alexander[3] obtained by far the best results in the treatment of this condition by the use of the immune rabbit serum in conjunction with sulfanilamide. Of twenty-six patients who lived forty hours or more, 17 recovered, representing a mortality rate of only 35 per cent. In this connection it is interesting to mention that Silverthorne and Brown[8] used immune serum from guinea pigs and rabbits in the treatment of *H. influenzae* meningitis. One of these patients treated with their immune rabbit serum and sulfapyridine recovered. A large number[16] of recoveries were also reported by Hoyne.[9] This author, however, fails to give the number of unsuccessfully treated patients.

The role of chemotherapy as an adjunct to treatment with type-specific antibodies is not yet fully understood. The observations of Lindsay, Rice, and Selinger[1] are of interest. These authors reported a series of 108 cases of *H. influenzae* meningitis. One group of patients was treated with specific serum and complement; the mortality rate was 83 per cent. The other group of thirteen patients received in addition sulfanilamide and sulfapyridine; the mortality rate was only 54 per cent. This suggests that chemotherapy is of value as an adjunct to serum treatment. Experimentally, Povitzky[10] in 1937 found that in mice the combined use of immune serum and prontosil resulted in a lower mortality rate than treatment with either agent alone.

The relative value of the various sulfamido compounds in the treatment of *H. influenzae* meningitis is not fully elucidated. Preliminary in vitro studies on the effects of these compounds upon *H. influenzae* in spinal fluid (according to a technique described elsewhere[11]) revealed that sulfanilamide, sulfapyridine, sulfathiazole, and sulfadiazine may cause loss of viability of this organism. Furthermore, the results

of these experiments suggest that sulfanilamide is somewhat less effective than the other drugs. In 1939, Pittman[12] showed that sulfapyridine definitely protected mice against *H. influenzae* (non-type-specific).

The action of sulfamido compounds on *H. influenzae* needs further experimental and clinical investigation before it can be decided which of the compounds will be the drug of choice in the treatment of *H. influenzae* meningitis. The final analysis naturally rests with the clinical results obtained. The presence of growth factors and sulfamido inhibitors in spinal fluid of patients with *H. influenzae* meningitis and their relation to the effectiveness of chemotherapy also require further study.

Relationship Between Free Anti-H. Influenzae Antibodies in the Blood and Presence of H. Influenzae or Its Specific Soluble Substance in the Spinal Fluid of Patients With H. Influenzae Meningitis.—In order to determine whether the presence of free antibodies in cases of *H. influenzae* meningitis following injection of immune rabbit serum could be used as a reliable criterion for adequacy of specific serum treatment, the following studies were carried out. The presence of antibodies in blood serum and spinal fluid was determined by means of the capsular swelling reaction, according to the method of Alexander,[3] using a formaldehyde-treated specimen of spinal fluid from a patient with *H. influenzae* meningitis as the source of organisms. Furthermore, the spinal fluid was cultured and the presence of specific-soluble substance determined as described. In two cases of *H. influenzae* meningitis, antibodies were present in the blood at a time when specific-soluble substance and viable *H. influenzae* could be demonstrated in the spinal fluid. Antibodies were not present in the spinal fluid. This observation was made on three consecutive days with identical results. Thus, there was ample time for the antibodies to act upon the organisms. Whether this finding is an exception remains to be seen. For this reason, until more reliable criteria in regard to adequacy of serotherapy are available, it seems absolutely necessary to follow these cases of *H. influenzae* meningitis carefully by means of repeated examinations of the cerebrospinal fluid and not to rely solely on the examination of the blood in regard to the presence of antibodies. Furthermore, at the present time it seems advisable to use relatively large quantities of specific antibodies over relatively long periods of time. On the other hand, it should be kept in mind that the injection of large amounts of immune serum at a time when much specific-soluble substance is still present in tissues and body fluids of these patients may have some undesirable effect.

One more point deserves a very brief discussion. In view of the relatively high incidence of transitory improvements with subsequent relapses (both clinical and bacteriologic) in cases of *H. influenzae* meningitis, it seems indicated to keep these patients desensitized dur-

ing this critical period by means of repeated injections of small amounts of the respective serum. So that if after an interval of several days serotherapy again becomes necessary, no difficulty will be encountered in its administration.

SUMMARY

A study on sixty-two cases of *H. influenzae* meningitis of children was carried out.

1. The bacteriologic and immunologic diagnosis of *H. influenzae* meningitis of children is discussed. The demonstration of the specific-soluble substance of *H. influenzae* in the spinal fluid is described.

2. A study of the incidence of bacteremia revealed that *H. influenzae* was present in the blood in eleven out of seventeen cases.

3. In regard to the location of foci, it was found that in four cases *H. influenzae* was recovered from throat and bronchi, respectively. Laryngotracheobronchitis necessitated tracheotomy in two patients with *H. influenzae* meningitis. In three patients *H. influenzae* was present in the middle ear. In one case *H. influenzae* septicemia with purulent arthritis preceded the meningitis by three weeks.

4. The results obtained by means of chemotherapy and serotherapy were as follows:

(a) Three patients received sulfamido compounds exclusively. One, treated with sulfathiazole, made a complete recovery.

(b) Two out of twelve patients who received anti-*H. influenzae* horse serum in conjunction with sulfamido compounds recovered.

(c) Of seven patients, who received anti-*H. influenzae* rabbit serum in conjunction with sulfamido compounds, four made a complete recovery. One of these patients had two attacks (relapse?) of *H. influenzae* meningitis with an interval of six weeks.

5. Following treatment with anti-*H. influenzae* rabbit serum, antibodies were demonstrated in the blood of two patients at a time when viable organisms and specific-soluble substance of *H. influenzae* were present in the spinal fluid. The importance and significance of this finding is discussed.

6. It is suggested to keep these patients desensitized to the therapeutic serum for several weeks until, as far as it is possible to judge, permanent recovery has been established.

The author wishes to express his sincere appreciation to Dr. Douglas P. Arnold, Chief of Staff of the Children's Hospital for his interest and many valuable suggestions, and to the members of the staff, whose cases were incorporated in this report.

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THE CHEMOTHERAPY OF INFANTILE DIARRHEA: A COMPARISON OF SULFATHIAZOLE AND SULFAGUANIDINE

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BECAUSE of the conflicting reports of the efficacy of sulfathiazole[1] and sulfaguanidine[2] in the treatment of infantile diarrhea, thirty-one infants admitted to Duke Hospital during the summer of 1941 with diarrhea were given sulfonamide therapy in addition to the routine basic treatment.* Sixteen of these patients were treated with sulfathiazole and fifteen with sulfaguanidine from the day of admission to the fourth or fifth day after their diarrhea and all symptoms and signs of infection, if present, had ceased (Table I). The infants under

TABLE I

TOTAL PATIENTS TREATED ACCORDING TO TYPE OF DIARRHEA

	TOTAL NUMBER OF PATIENTS	TREATED WITH SULFATHIAZOLE		TREATED WITH SULFAGUANIDINE	
		NUMBER OF PATIENTS	AVERAGE DAYS TO CURE	NUMBER OF PATIENTS	AVERAGE DAYS TO CURE
Parenteral diarrhea	15	8	4.7	7	3.8
Bacillary dysentery	16	8	4.4	8	3.8

1 year of age in the sulfathiazole group received 1 Gm. (gr. xv) on admission and 0.25 Gm. (gr. iv) q.4 h., and those in the sulfaguanidine series were given 2 Gm. (gr. xxx) on admission and 0.5 Gm. (gr. viiss) q.4 h. The doses of each of these drugs were doubled for infants over the age of 1 year. The only toxic reactions were in two patients whose fever was apparently prolonged by sulfathiazole; their temperatures became normal when the drug was stopped.

Clinically sixteen of the thirty-one infants had bacillary dysentery and fifteen had parenteral diarrhea; i.e., they had infection elsewhere, usually upper respiratory infections (Tables II and III). However, no

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*The routine basic treatment which all diarrhea patients received was: (1) one-sixth molar sodium lactate as indicated by the admission CO_2 combining power, one-half the dose being given intravenously and one-half subcutaneously; (2) nothing by mouth for the first 24 hours except Ringer's solution and weak tea as desired; (3) after twenty-four hours equal parts of evaporated milk and water with 0.75 per cent lactic acid and 5 per cent Casec was offered in amounts furnishing 20 calories per kilogram of body weight, and if this was taken, the quantity was increased by 20 calories per kilogram every second day until the caloric requirements were attained; (4) 5 per cent dextrose intravenously and other parenteral fluids as indicated by the degree of dehydration up to 30 c.c. per kilogram of body weight in 24 hours; (5) blood transfusions following hydration, if indicated; (6) daily maintenance oral doses of thiamin chloride and ascorbic acid.

TABLE II

SIXTEEN PATIENTS TREATED WITH SULFATHIAZOLE

SEX	RACE	AGE (MO.)	CLINICAL DIAGNOSIS	DAILY NUMBER OF STOOLS PRIOR TO ADMISSION	DEGREE OF DEHYDRATION	SULFATHIAZOLE (GM.)			DAYS UNTIL CURE
						ADMISSION DOSE	Q.4 H. DOSE	TOTAL DOSE	
F	C	5	Dys.	6 to 8 (1 week)	Marked	0.3	0.1	3.3	4
F	W	3	Dys.	Many (4 days)	Marked	0.1	0.1	3.1	4
F	C	24	P.D.	Many	Marked	1.0	0.3	13.6	3
M	W	14	P.D.	15 to 20 (24 hours)	Marked	1.0	1.25	13.0	3
M	W	22	P.D.	12 (1 week)	Marked	2.0	0.3	9.2	3
F	W	9	P.D.	6 to 7	Marked	1.0	0.2	5.8	4
F	C	5	P.D.	Unknown	Marked	0.15	0.15	7.2	7
F	C	1.5	Dys.	6 to 7	Marked	0.15	0.15	5.4	6
F	C	5	P.D.	Unknown	Marked	0.15	0.15	7.2	11
M	W	8	Dys.	7 to 10	Marked	0.5	0.15	7.7	4
M	W	8	Dys.	20	Marked	0.5	0.15	5.0	4
F	W	18	P.D.	5 (24 hours)	Moderate	1.5	0.25	7.5	2
M	W	3	Dys.	7 to 10 (1 week)	Moderate	0.25	0.1	2.05	4
M	C	2	Dys.	12 (2 mo.)	Slight	0.3	0.1	2.1	5
M	W	2	P.D.	8 to 9	Slight	0.5	0.1	3.5	3
M	W	9	Dys.	4 to 5 (4 weeks)	Slight	0.5	0.25	9.5	4

TABLE III

FIFTEEN PATIENTS TREATED WITH SULFAGUANIDINE

SEX	RACE	AGE (MO.)	CLINICAL DIAGNOSIS	DAILY NUMBER OF STOOLS PRIOR TO ADMISSION	DEGREE OF DEHYDRATION	SULFAGUANIDINE (GM.)			DAYS UNTIL CURE
						ADMISSION DOSE	Q.4 H. DOSE	TOTAL DOSE	
M	W	2.5	Dys.	10 to 12 (4 days)	Marked	1.0	0.25	7.0	3
F	C	13	Dys.	10 to 15 (5 days)	Marked	1.0	0.3	17.2	4
F	W	2	P.D.	Unknown	Marked	1.0	0.3	13.6	6
M	W	8	Dys.	20	Marked	1.0	0.3	10.0	5
M	C	5	Dys.	5 to 6 (2 weeks)	Marked	0.2	0.2	7.4	6
F	C	2.25	Dys.	6 to 7 (2 days)	Marked	0.4	0.15	4.9	2
M*	C	4	P.D.	16 (4 days)	Marked	0.4	0.2	2.8	7
M†	C	2.5	Dys.	25 (24 hours)	Marked	0.2	0.2	3.8	5
M‡	W	5	P.D.	Many (2 weeks)	Marked	1.0	0.3	10.0	6
M	W	9	Dys.	Many	Moderate	1.0	0.5	34.0	3
F	W	16	P.D.	Many	Moderate	2.0	0.3	11.0	4
F	C	24	P.D.	8 to 9	Moderate	2.0	0.7	31.4	3
M	W	4	Dys.	4 to 5 (1 week)	Moderate	0.5	0.25	12.5	4
M	W	8	P.D.	8 to 15 (3 weeks)	Slight	1.0	0.25	10.0	3
F	C	24	P.D.	Many	Slight	2.5	0.8	16.9	3

*This patient also received 4.8 grams of sulfathiazole.
†This patient also received 3.1 grams of sulfathiazole.
‡This patient also received 6.45 grams of sulfathiazole.

pathogenic bacteria were isolated from the stools of either group, although they were cultured daily for three days after admission.

Eight of the bacillary dysentery group were given sulfathiazole and eight received sulfaguanidine. Of the patients who received sulfaguanidine, one who was not improving was later given sulfathiazole with marked benefit. Of the parenteral diarrhea series, eight were treated with sulfathiazole and seven received sulfaguanidine. Of the patients receiving sulfaguanidine, two who showed no improvement were changed to sulfathiazole and immediately improved. As shown in Table I, except for the three infants who did not improve on sulfaguanidine, the two drugs were equally effective in both the dysentery and parenteral diarrhea cases.

TABLE IV

DISTRIBUTION OF PATIENTS ACCORDING TO DEGREE OF DEHYDRATION

DEHYDRATION	TREATED WITH SULFATHIAZOLE		TREATED WITH SULFAGUANIDINE	
	NUMBER OF PATIENTS	AVERAGE DAYS TO CURE	NUMBER OF PATIENTS	AVERAGE DAYS TO CURE
Marked	11	4.8	9	4.8
Moderate	2	3.0	4	3.5
Slight	3	4.3	2	3.0
Results	16	4.44	15	4.26

TABLE V

PATIENTS WITH TYPHOID AND PARATYPHOID TREATED WITH SULFATHIAZOLE AND SULFAGUANIDINE

SEX	RACE	AGE (MO.)	CLINICAL DIAGNOSIS	NUMBER OF STOOLS PRIOR TO ADMISSION	DEGREE OF DEHYDRATION	SULFONAMIDE (GM.)			DAYS UNTIL CURE
						ADMISSION DOSE	Q.4 H. DOSE	TOTAL DOSE	
F*	W	3	Typhoid	16 (4 days)	Marked	0.5	0.15	7.3	7
F*	W	7	Paratyphoid	Many	Marked	0.3	0.1	4.8	3
M†	W	0.5	Paratyphoid	7 to 8 (2 weeks)	Marked	0.5	0.25	17.25	3
M†	C	4	Paratyphoid	Many (20 hours)	Moderate	2.0	0.25	19.0	4

*These patients received sulfathiazole.
†These patients received sulfaguanidine.

When the cases are analyzed according to the degree of dehydration (Table IV), sulfathiazole and sulfaguanidine were equally effective in all three groups.

In addition to these thirty-one cases of diarrhea treated with sulfonamide drugs, four patients were admitted with histories of severe diarrhea and died in collapse within a few hours of admission. They are not included in this series because they did not live long enough to be given sulfonamide therapy.

One case of typhoid fever and one of paratyphoid A were treated with sulfathiazole, and two paratyphoid A patients received sulfaguanidine (Table V). The sulfonamides seemed to have been beneficial in checking the diarrhea.

CONCLUSION

Both sulfathiazole and sulfaguanidine, in the doses used, were equally effective in the treatment of infantile diarrhea of the clinical bacillary dysentery and parenteral diarrhea types.

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A TUBERCULOSIS SURVEY OF HOUSEHOLD GROUPS

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THE results of a survey conducted in private practice for the purpose of preventing or terminating the exposure of children to patients with open tuberculosis were reported in 1937.[1] Continuance of this program to June, 1941, has resulted in an initial survey of 4,251 patients representing a total of 1,444 households. This group of patients was comprised of 2,161 children, 1,987 parents, and 103 domestic servants, relatives, and other adults (Table I). The survey included the entire personnel of 683 households. Of the remaining 761 partially surveyed units, 621 were represented by children and only one parent, and 140 were represented solely by children.

Follow-up observations, covering an average period of slightly more than three years, were also made on 654 children and 242 adults who reacted negatively to the first Mantoux test they received (Table IV). The combined data derived from the initial survey and from the follow-up study forms the basis of this report.

The survey included routine applications of Mantoux tests using 0.1 mg. of old tuberculin. Clinical and x-ray studies were recommended to all infected patients, but in instances where the family income was low, x-ray examinations of tuberculin sensitive adults, who appeared to be well, were not insisted upon provided the children with whom they were residing had negative Mantoux tests. The absence of infection in these children was interpreted as satisfactory evidence that their infected adult associates were not disseminating tubercle bacilli. This assumption was supported by the negative results of the many fluoroscopic studies that were used in lieu of the more expensive x-ray plates. If, however, the junior members of a household group were sensitive to tuberculin, a complete examination of each infected member of the unit was required.

THE RESULTS OF THE INITIAL SURVEY

Some of the results of the initial survey are summarized in Table I. The Mantoux tests applied to the children included in this study disclosed sensitiveness to tuberculin in 3.2 per cent of the group. Of the 1,987 parents and 103 maids, relatives, and other adults with whom these children were residing, approximately 55 per cent (1,144) were sensitive to tuberculin. However, in spite of an average of six years of intimate contact with 1,144 infected adults living in many of the homes

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represented in this study, nearly 97 per cent of the group of 2,161 tested children had escaped infection with tubercle bacilli. This observation is interpreted as evidence that the form of tuberculosis that produces sensitiveness to tuberculin, namely the so-called primary tuberculosis, is a relatively noncontagious form of the disease. Apparently tuberculosis must progress beyond the primary phase of its development before it becomes an important menace to the health of the public.

The initial survey of 1,444 household groups disclosed information relative to thirty-two tuberculous adults to whom the members of different units had been exposed (Table I). As a rule this information was obtained after routine tuberculin tests had revealed the presence of sensitiveness to tuberculin in individuals who knew they had associated in the past with tuberculous patients but were unaware of the fact they had been infected. These tuberculous patients obtained their diagnoses from sources that were entirely independent of this survey, but in several instances the extent to which they had spread their infection among their intimate associates had not been investigated thoroughly.

TABLE I

THE RESULTS OF THE INITIAL SURVEY OF 1,444 HOUSEHOLDS

	AVERAGE AGE (YR.)	TOTAL NUMBER	PER CENT AND NUMBER POSITIVE TO 0.1 MG. OF OLD TUBERCULIN	PATIENTS WITH PULMONARY TUBERCULOSIS*	
				DISCOVERED BY THIS SURVEY	DIAGNOSED INDEPENDENT OF THIS SURVEY
Children	6.3	2,161	3.2 (70)	2	32
Parents	35.6	1,987	54.7 (1,087)		
Maids,* relatives and other adults	46.8	103	55.3 (57)		

*In intimate contact with different household groups included in this study.

The initial survey was directly responsible for the detection of two additional patients with pulmonary tuberculosis. One of these patients, an elderly adult, was discovered after routine testing had disclosed sensitiveness to tuberculin in an infant 6 months of age who was being treated for a sublingual ulcer. This tuberculous adult and the baby he infected lived in adjoining apartments. The infant died of miliary tuberculosis at the age of 8 months. This death was the only one that occurred during the average follow-up period of three years in the group of seventy children who reacted positively to the first Mantoux test they received.

The second tuberculous adult who was discovered in the course of the initial survey was the only infected member of a family of three (Table II). X-ray study of this patient, the mother, disclosed a pulmonary lesion which was diagnosed as pulmonary tuberculosis during the following four months. After the diagnosis was fully established,

the patient entered a sanatorium for treatment, but in spite of the special care she received, a thoracoplasty was required in 1938. Mantoux tests were reapplied to her husband and son in March of that year and were negative in each instance. In 1939 the mother returned to her home and one year later she bore a second child. On rechecking the family after eleven additional months had elapsed, during which time the mother remained at home, no evidence of infection was found in the other three members of the family.

TABLE II

RECORD OF A FAMILY IN WHICH PULMONARY TUBERCULOSIS WAS DISCOVERED BY THE INITIAL SURVEY

MEMBERS OF FAMILY	AGE (YR.)	RESULTS OF INITIAL MANTOUX TESTS (3/37)	RESULT OF INITIAL X-RAY AND CLINICAL STUDY (6/37)	RESULTS OF SECOND MANTOUX TESTS (3/38)	RESULT OF THIRD MANTOUX TESTS (4/41)
Mother	24	Pos.	Pulmonary tuberculosis*		
Father	26	Neg.	0	Neg.	Neg.
Son	1.5	Neg.	0	Neg.	Neg.

*Thoracoplasty in 1938; mother returned to her home in May, 1939; second child born May, 1941; infant's Mantoux test was negative April, 1941.

TABLE III

THE COMPLETELY SURVEYED HOUSEHOLD GROUPS

PARENTS			CHILDREN		
AVERAGE AGE (YR.)	TOTAL NUMBER	PER CENT SENSITIVE TO OLD TUBERCULIN	AVERAGE AGE (YR.)	TOTAL NUMBER	PER CENT AND NUMBER SENSITIVE TO OLD TUBERCULIN
Reaction to 0.1 mg. of Old Tuberculin Negative For Each Parent					
34.6	304	0	5.7	246	2.5 (6)
Reaction to 0.1 mg. of Old Tuberculin Negative for One Parent, Positive for Other Patient					
34.8	608	50	5.7	507	1.6 (8)
Reaction to 0.1 mg. of Old Tuberculin Positive for Each Parent					
38.5	454	100	6.7	404	6.9 (28)

The records of this family disclose the manner in which early diagnosis and adequate therapy may succeed in preventing the spread of tuberculous infection within a family and illustrate the potentially serious disease that may be overlooked occasionally if complete examinations of tuberculin-sensitive adults are omitted because their intimate associates react negatively to the Mantoux test, an economical expedient that was frequently resorted to in this survey.

The results of the Mantoux tests applied to the members of the 683 completely surveyed households are recorded in Table III. In this table the family units are separated into three groups on the basis of

the number of infected parents living in each of these 683 homes. This method of tabulation was used in order that observations on children who were residing with either two uninfected parents, with one uninfected and one infected parent, or with two infected parents might be compared.

The incidence of sensitiveness to tuberculin was higher for the children who were residing with uninfected parents than it was for the children from homes that included one infected parent. The highest percentage of positive Mantoux tests in children was found in those who were residing in homes where two infected parents were present. The moderate excess number of infected children in this group of homes is statistically significant when correction is made for the difference in average age.

These observations are difficult to interpret. They show that tuberculin-sensitive parents usually fail to infect their children, and they suggest that environmental conditions which raise the incidence of positive Mantoux tests in groups of parents to 100 per cent also produce moderate elevation in the average prevalence of tuberculous infections in their children.

THE FOLLOW-UP STUDY

The follow-up study that was incorporated in this survey resulted in observations on 654 children and 242 parents who reacted negatively to the first Mantoux test they received (Table IV). The period these patients were traced averaged approximately three years, during which 2.6 per cent of the children and 14.5 per cent of the parents became sensitive to tuberculin. The annual rate at which these adults had acquired infections with tubercle bacilli amounted to 4.4 per cent. This annual primary tuberculous infection rate is more than five times that experienced during the same calendar years by the children who were traced. Since this difference between the two age groups is statistically significant, it seems obvious that the current need for protection from infection is distinctly higher for the senior than it is for the junior members of groups that are comparable to one surveyed in this study.

Investigation designated to locate the sources from which seventeen of the traced children acquired infecion with tubercle bacilli resulted in the identification of six patients with pulmonary tuberculosis. This group of newly discovered tuberculous individuals included two mothers, a grandmother, an aunt, a maid, and a daughter.

This daughter was the only member of a family of six to become sensitive to tuberculin following a period of six weeks of exposure to an aunt in 1926. This child remained in excellent health throughout the succeeding five years, during which time her x-ray plates were repeatedly negative. In the fall of 1931 she had a pulmonary hemorrhage at the age of 16 years, and studies made at this time revealed a small tuberculous lesion in the subapical portion of the right lung. She re-

mained in her home, but throughout the ten years that have elapsed since her pulmonary hemorrhage occurred the remaining members of this family have repeatedly reacted negatively to tuberculin.

The five additional tuberculous adults who were discovered in the course of the follow-up study probably were responsible for infecting six members of the group of seventeen children who acquired sensitiveness to tuberculin during the average period of three years that they were traced. The patients responsible for infecting the remaining eleven members of this group were not identified.

TABLE IV

RESULTS OF THE FOLLOW-UP STUDY OF CHILDREN AND ADULTS WHO REACTED NEGATIVELY TO THE FIRST TUBERCULIN TEST THEY RECEIVED

	CHILDREN	PARENTS
Average initial age (yr.)	5.9	34.1
Length of follow-up study (yr.)	3.2	3.1
Total number traced	654	242
Number that became sensitive to 0.1 mg. of old tuberculin	17	35
Per cent that acquired infection	2.6	14.5
Annual primary tuberculous infection attack rate (%)	0.8	4.4
Number that died of tuberculosis following infection	0	0
Number of open cases of tuberculosis discovered	6	0

Investigations made for the purpose of locating the open cases who infected 35 members of the group of 242 traced adults failed to result in the discovery of previously undiagnosed tuberculous patients but did succeed in eliciting a history of definite exposure to nine patients with advanced disease. The remaining 26 adults who acquired infection with tubercle bacilli during the course of the follow-up study were totally unaware of having had any contact with tuberculous patients.

The initial survey of 4,251 individuals and the follow-up study of 896 patients who reacted negatively to the first Mantoux test they received were directly responsible for the discovery of a total of eight open cases of pulmonary tuberculosis (Tables I and IV). In this respect the follow-up study of the group of 654 children was especially effective. It led to the detection of six of these eight tuberculous adults.

The manner in which the follow-up study led to the detection of patients with open tuberculosis can be illustrated by relating a typical experience. Initial Mantoux tests applied to the members of a family of four disclosed two tuberculin sensitive parents residing with two uninfected children (Table V). X-ray studies were made at this time of these infected parents and were negative in each instance. Approximately two years later the younger of the two children, who was 6 years old, developed erythema nodosum. Mantoux tests were reapplied to this patient and also to her brother, who was apparently well, and in each instance a positive reaction was obtained. These findings combined

TABLE V

FOLLOW-UP STUDY THAT RESULTED IN THE DISCOVERY OF TWO ADULTS WITH OPEN TUBERCULOSIS

	AGE (YR.)	RESULT OF FIRST TUBERCULIN TEST (9/36)	RESULT OF FIRST X-RAY STUDY (9/36)	RESULTS OF LATER TUBERCULIN TESTS (8/38)	RESULTS OF LATER CLINICAL AND X-RAY STUDIES (9/38)	ADDITIONAL STUDIES (3/41)
Father	38	Pos.	Neg.		Neg.	Neg.
Mother	35	Pos.	Neg.		Neg.	Neg.
Son	5	Neg.		Pos.*	Neg.	Neg.
Daughter	4	Neg.		Pos.†	Primary tuberculous; pulmonary infiltration	Infiltration has resolved
Relatives Who Frequently Visited This Family						
Miss D.	25			Pos.	Neg.	Neg.
Miss S.	32			Pos.	Neg.	Neg.
Mr. S.	54			Pos.	Neg.	Neg.
Mrs. M.	65			Pos.	Neg.	Neg.
Mrs. S.	52			Pos.	Chronic pulmonary tuberculosis and positive sputum	In sanatorium
Mrs. D.	60			Pos.		

*Was apparently well.

†Erythema nodosum was the only symptom present at that time.

with the antecedent knowledge that these children reacted negatively to previous tuberculin tests proved that these infections were acquired during an interval of two years.

Following the discovery of a spread of infection with tubercle bacilli in this household group, each member of the unit received x-ray studies which disclosed a pulmonary infiltration in the child with erythema nodosum but were negative for the remaining three members of the family. Six relatives who frequently visited this home were also examined, and this extension of the survey disclosed open tuberculosis in two elderly adults, a grandmother and her sister.

The follow-up study failed to prevent the spread of infection in this family but it did succeed in terminating intimate contact with open cases of tuberculosis before irreparable damage had been done.

THE PRIMARY TUBERCULOUS INFECTION ATTACK RATE

In addition to detecting eight tuberculous adults, this study also disclosed interesting information relative to fluctuations that may characterize the primary tuberculous infection attack rate at different ages.

Before discussing this point, it may be appropriate to recall that a first infection with tubercle bacilli produces an enduring sensitiveness to tuberculin which subsequent reinfections do not alter in any manner that can be demonstrated. Consequently, Mantoux tests applied to a group of patients reveal the primary infections various individuals have acquired but disclose no information relative to the reinfections that may have occurred in the group.

If the primary tuberculous infection attack rate is sufficiently high to render the majority of children sensitive to tuberculin, study of the manner in which the primary infection rate may vary as age advances is automatically limited to the period of childhood. Obviously, therefore, information relative to the fluctuations that may characterize the primary infection attack rate operating throughout a major portion of the usual span of human life must be obtained under circumstances that enable a high percentage of the child population to reach maturity without being infected. The group included in this study satisfies this requirement.

TABLE VI

THE PER CENT OF INFECTED INDIVIDUALS IN GROUPS REPRESENTING EACH ADVANCE OF FIVE YEARS IN AVERAGE AGE

AGE (YR.)	TOTAL NUMBER OF PATIENTS IN EACH AGE GROUP	SENSITIVE TO 0.1 MG. OLD TUBERCULIN		INCREASE IN INFECTION PER FIVE-YEAR INCREASE IN GROUP AGE
		NUMBER	PER CENT	PER CENT
0- 4	994	16	1.6	1.6
5- 9	747	26	3.3	1.7
10-14	326	18	5.5	2.2
15-19	82	8	9.8	4.3
20-24	119*	28	23.5	{13.7
25-29	335	145	43.3	{19.8
30-34	545	271	49.7	6.4
35-39	539	318	59.0	9.3
40-44	321	222	69.2	10.2
45-49	139	91	65.5	
50-80	104	70	67.3	

*Twelve of these patients were unmarried adults. In Table I they are included with the children.

The per cent of infected individuals in successive subgroups representing each advance in average age amounting to five years is recorded in Table VI and in Chart 1, Curve *A*. In this series of patients the incidence of sensitiveness to tuberculin increased progressively until it reached a maximum level of 69.2 per cent in the group that represented the early forties and then declined slightly.

The actual or absolute increase in the percentage of infected individuals that accompanied advancing age did not occur at a rate that remained uniform throughout the four decades these changes were taking place (Table VI, Column 5). In general, the primary tuberculous infection attack rate per age group increased from 1.6 to 4.3 per cent during childhood. At the termination of this age period the infection rate was accelerated abruptly and reached a maximum level of 19.8 per cent during the latter half of the twenties. Subsequently it declined but failed to subside to the low level observed here for the period of childhood. These observations agree with the findings of the follow-up study in showing the primary tuberculous infection attack rate to be higher for adults than for children. Graphic representation of the

general pattern of the fluctuations displayed by the tuberculous infection attack rate as group age advanced is shown by curve *B* on Chart 1.

Since the fortuitous antecedent absence or presence of tuberculous infection rather than inherent factors peculiar to such contaminations determine whether they are primary or reinfection in character, some basis exists for suspecting that the reinfections acquired during the adult period of life may greatly outnumber those acquired during childhood. Regardless of whether this assumption is correct or erroneous, it seems obvious that adults as well as children can profit greatly from measures that provide protection from infection with tubercle bacilli.

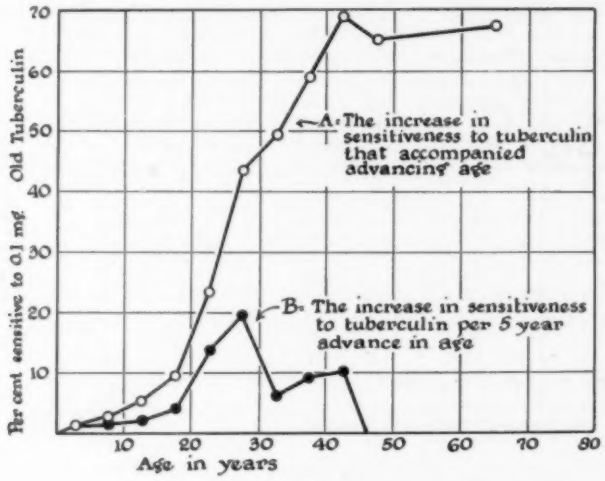

Chart 1.

SUMMARY

An initial survey of 4,251 patients (2,161 children and 2,090 adults) representing 1,444 households resulted in the discovery of two patients with pulmonary tuberculosis and produced information relative to 32 additional tuberculous adults to whom the members of different home units had been exposed.

A follow-up study of three years' duration on 654 children who reacted negatively to the first Mantoux test they received resulted in the identification of six adults with pulmonary tuberculosis.

A comparable follow-up study on 242 adults failed to discover previously unrecognized tuberculous patients.

With respect to the discovery of patients with open tuberculosis, the follow-up study on children was particularly effective.

The initial survey and the follow-up study revealed a higher primary tuberculous infection attack rate for adults than for children.

CONCLUSION

Physicians can make an important contribution to the control and eradication of tuberculosis by including tuberculosis surveys and follow-up studies in their private practices.

Adults as well as children can profit from measures designed to prevent infection with tubercle bacilli.

Primary tuberculosis is relatively noncontagious.

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TREATMENT OF WHOOPING COUGH BRONCHOPNEUMONIA

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WHOOPING cough has long been known as having a high mortality in infancy. It has a case fatality rate of about 25 per cent in infants under 1 year of age and of about 10 per cent in infants in the second year of life.[1] In the United States it takes over 6,000 lives annually. The majority of these are due to a complicating bronchopneumonia.

In an effort to reduce the mortality rate, a study was undertaken in January, 1940, to determine the value of hyperimmune pertussis serum in the treatment of whooping cough bronchopneumonia. The serum was given intravenously or intramuscularly on admission in doses of 2½ to 3 c.c. per pound of body weight. Hyperimmune serum was prepared after the method of Kendrick.[2] By November, 1940, thirty consecutive cases had been treated with a mortality of 20 per cent. There were fourteen cases under 1 year of age with four deaths, ten cases from 1 to 2 years with one death, and six cases over 2 years with one death. In only nine patients the temperature dropped to normal within twenty-four to seventy-two hours after its use. Although this was an improvement over our previous experience, the only conclusion to be drawn was that the serum had acted as a good supportive measure and not as a specific cure.

Sixteen serum-treated patients also received sulfapyridine after it became apparent that serum was not specific. The drug was given orally in doses of ⅙ gr. per pound of body weight every four hours. There were nine cases under 1 year of age with three deaths, five from 1 to 2 years with no deaths, and two cases over 2 years of age with one death. In only four patients did a normal temperature occur within four days after its use. Although the series was small, the conclusion drawn was that sulfapyridine was of limited value. One reason for this result may have been the fact that pneumococci were recovered in only two out of eight cases in which sputum was cultured.

In November, 1940, as a result of favorable reports in the treatment of other types of pneumonia, the use of sulfathiazole was begun. It was given in daily doses of 1 to 2 gr. per pound of body weight. One-fourth to all of the daily dose was given on admission, according to the urgency of the need, and then one-sixth of the calculated amount was given every four hours. The drug was given by mouth in the form of an emulsion. For each dose of sulfathiazole an equal amount of sodium bicarbonate

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was given. In the ensuing nine months to August, 1941, seventy-seven consecutive cases of whooping cough bronchopneumonia were treated with sulfathiazole with the unprecedented low mortality of 4 per cent. There were thirty-two cases under 1 year of age with two deaths, twenty-four cases from 1 to 2 years with one death, and twenty-one cases over 2 years of age with no deaths. These statistics do not include deaths that occurred within twenty-four hours after admission to the hospital.

TABLE I

HYPERIMMUNE SERUM IN THE TREATMENT OF WHOOPING COUGH BRONCHOPNEUMONIA

AGE (YR.)	NUMBER TREATED WITH SERUM	NUMBER BENEFITED IN TWENTY-FOUR TO SEVENTY-TWO HOURS	PER CENT BENEFITED	DEATHS	MORTALITY RATE (PER CENT)
0 to 1	14	2	14	4	28.5
1 to 2	10	3	30	1	10
Over 2	6	4	66	1	16
Totals	30	9	30	6	20

TABLE II

SULFAPYRIDINE IN THE TREATMENT OF WHOOPING COUGH BRONCHOPNEUMONIA

AGE (YR.)	CASES TREATED WITH SULFAPYRIDINE	NUMBER BENEFITED WITHIN FOUR DAYS	PER CENT BENEFITED	DEATHS	MORTALITY RATE (PER CENT)
0 to 1	9	3	33	3	33
1 to 2	5	1	20	0	0
Over 2	2	0	0	1	50
Totals	16	4	25	4	25

TABLE III

SULFATHIAZOLE IN THE TREATMENT OF WHOOPING COUGH COMPLICATED BY BRONCHOPNEUMONIA

AGE (YR.)	CASES	DEATHS	MORTALITY RATE (PER CENT)
Under 1	32	2	6¼
1 to 2	24	1	4
Over 2	21	0	0
Totals	77	3	4

In evaluating sulfathiazole therapy in this series, a number of interesting observations stand out. For the most part, the drug was well tolerated by even the youngest babies. No complications resulted from its use. The blood concentrations necessary for effective results were surprisingly low, averaging 2 to 3 mg. per 100 c.c. of blood. Often there was marked improvement with only traces of sulfathiazole in the blood. Improvement as measured by drop in temperature did not occur by crisis but rather by lysis. The average case required four days for a return of the temperature to normal. The average length of treatment

with sulfathiazole was nine days. In sharp contrast to results with previous therapy, 80 per cent of the cases treated with sulfathiazole definitely responded to the drug.

It would be incomplete to conclude this study of the treatment without commenting briefly on other important adjuncts of therapy that were employed. Special nurses were used during the most critical periods. The babies were hand fed. Sedatives were given as indicated. The diets were fortified with large amounts of vitamins A, B, C, and D. Oxygen and parenteral fluids were administered when necessary.

SUMMARY

1. Thirty consecutive patients with whooping cough bronchopneumonia were treated with large doses of hyperimmune pertussis serum with a mortality rate of 20 per cent. In only nine cases did the temperature become normal within twenty-four to seventy-two hours.

2. Sixteen patients were treated with sulfapyridine with a mortality rate of 25 per cent. Only four cases responded to the drug within four days.

3. Seventy-seven consecutive patients were treated with sulfathiazole with a mortality rate of 4 per cent. There were thirty-two cases under 1 year of age with two deaths, twenty-four cases from 1 to 2 years with one death, and twenty-one cases from 2 to 7 years of age with no deaths. Improvement did not come by crisis but by lysis, the temperature of the average patient returning to normal in four days.

4. Eighty per cent of the patients responded to sulfathiazole therapy.

5. The blood concentration of sulfathiazole needed for good results was relatively low, about 2 to 3 mg. per 100 c.c. of blood.

CONCLUSIONS

1. Sulfathiazole reduced the mortality to an unprecedented low figure.

2. Sulfapyridine was found to be of limited value.

3. Hyperimmune pertussis serum was found to exert no specific effects in the treatment but could be recommended as good supportive therapy.

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STUDIES OF THE PHYSICAL CHARACTERISTICS OF SELECTED CHILDREN IN MADRID, SPAIN, IN 1941

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IN CONNECTION with a survey of the nutritional status of a population group in Madrid, Spain, conducted during June, July, and August of 1941, an opportunity was afforded to obtain data regarding the growth and developmental status of the children included in the study. The report of a similar study in Marseilles, France, has been recently published.[1] Since the general purposes of the two studies and the methods used in them were identical, the present report is limited to the presentation of the data obtained in Spain, together with the pertinent differences in the environmental conditions of the two groups. This report deals with seventy-five boys and eighty-five girls under the age of 10 years and 6 months, recruited entirely from the family series of the nutrition survey. These children are described in respect to body measurements, certain clinical findings, and the observations made upon roentgenograms. Data on children with organic disease have been excluded. The findings in this series are compared with those from groups previously studied in a comparable manner. It should be emphasized that there is no intention of speculating on the causes of any differences found between the study and the reference series; the purpose is merely to recognize and define any such differences. The primary object of the initial survey was to obtain data to serve as a base line from which to measure progress of growth under known dietary and health conditions.

These children all came from families living in an industrial suburb of Madrid, and in general fell into the lower economic levels. They have been subjected to a marked dietary restriction for a period of one and a half years or longer. In general, the dietary intake *at the time of the survey* may be characterized as definitely below maintenance levels in caloric value and calcium content, and relatively inadequate in protein, especially of animal origin. It was relatively adequate in iron, thiamine, ascorbic acid, and probably phosphorus; vitamin A, riboflavin, and pellagra-preventive value were low and may well have been

The studies and observations on which this report is based were conducted with the support and under the auspices of The Rockefeller Foundation Health Commission and with the collaboration of the "Dirección de Sanidad" of the Spanish Government. The authors are indebted to Harold C. Stuart, M.D., for assistance and advice in the organization of the study, analysis of data, and its preparation for publication.

below maintenance levels.* Since the ages of those reporting for examination were not controlled, it was necessary to divide these children into many age groups with small numbers in each, a deviation of three months from the birth date being allowed at all ages unless otherwise specified. The groups are too small to justify the study of distributions, and the data presented give only the means of the measurements.

We have been unable to find reports of studies of Spanish children suitable for use in the interpretation of the measurements derived from the children in Madrid. It is necessary to compare these children with groups that have been carefully studied by technically comparable procedures, even though racial factors may account for any or all of the differences encountered. Data obtained from studies of a small group of white children of North European stock, re-examined periodically over a period of from five to eight and one-half years at the Harvard School of Public Health,[2, 3] have been used as the standards for most measurements, because the techniques used in studying the children in Madrid were modeled after the Boston studies in so far as circumstances permitted. Comparison of some of the measurements with the results obtained in the Marseilles study of 1941[1] is also made. The data are presented so that they may be compared readily with other American and European standards by reference to the report of the Marseilles study.[1] In the case of all but two of the children included in this report, both parents were Spanish born.

Body Size and Build.—Four measurements of body size were taken at all ages: weight, chest circumference, span from finger tip to finger tip, and the bi-iliocristal pelvic breadth. Stature was measured as recumbent length of children under 3 years of age and as standing height of those of 3 years of age or more.

In Tables I and II are presented the means for these measurements for boys and girls, respectively, and the number of subjects entering the calculations at each age is given. In Charts 1 through 4 these means are plotted against the Boston norms and the means for Marseilles. Although the small number of subjects in each group makes it impossible to evaluate the statistical significance of the differences between the study and reference data at any one age, the consistency of some of these differences at successive ages and for both sexes makes them deserving of attention.

Chart 1 shows that the children in the Madrid series have a much lower average weight for age than do the Boston children. Most of the means for the former are two or more sigma below the means for the latter. The means for the Madrid series are also consistently below those for the Marseilles children.

*The analysis of dietary studies and results of tests for specific nutritional deficiencies will be reported later.

Table I

Means of Body Measurements for Boys

Age	Weight		Length or Height*		Span		Chest Circumference		Pelvic Breadth	
	Number of Cases	Mean (Kg.)	Number of Cases	Mean (Cm.)	Number of Cases	Mean (Cm.)	Number of Cases	Mean (Cm.)	Number of Cases	Mean (Cm.)
3 mo.	1	6.32	1	61.1	1	61.0	1	39.0	1	14.0
6 mo.	4	5.40	4	61.8	4	60.5	4	38.5	4	13.0
9 mo.	1	6.60	1	65.1	1	62.0	1	38.0	1	15.5
1 yr.	5	8.78	5	72.2	5	71.4	5	46.2	5	16.0
1½ yr.	2	7.94	2	72.0	2	69.0	2	44.2	2	14.0
2 yr.										
2½ yr.										
3 yr.	4	11.35	4	85.6	4	84.0	4	49.9	4	16.6
3½ yr.	2	11.20	2	84.0	2	86.5	2	50.8	2	17.3
4 yr.	4	12.71	4	89.3	4	90.4	4	50.6	4	16.8
4½ yr.	3	13.50	3	94.6	3	95.0	3	53.5	3	18.8
5 yr.	3	12.20	3	94.6	3	96.3	3	52.2	3	17.3
5½ yr.	3	17.03	3	107.2	3	102.3	2	55.0	1	22.5
6 yr.	3	12.67	3	96.2	3	96.0	3	51.2	3	17.5
6½ yr.	8	15.85	8	105.8	8	105.2	7	54.9	8	19.0
7 yr.	4	17.48	4	109.1	4	109.5	4	56.2	4	19.8
7½ yr.	5	16.80	5	106.9	5	104.8	5	53.7	5	19.3
8 yr.	5	19.03	5	111.3	5	111.2	5	58.4	5	21.6
8½ yr.	4	21.08	4	117.5	4	118.0	4	56.4	4	21.9
9 yr.	5	19.12	5	116.7	5	116.7	5	58.4	5	20.9
9½ yr.	1	23.22	1	124.1	1	128.0	1	64.0	1	23.0
10 yr.	8	22.90	8	122.2	8	122.9	8	63.4	7	21.1

*Up to 3 years of age, length; 3 years and over, height.

Table II

Means of Body Measurements for Girls

Age	Weight		Length or Height*		Span		Chest Circumference		Pelvic Breadth	
	Number of Cases	Mean (Kg.)	Number of Cases	Mean (Cm.)	Number of Cases	Mean (Cm.)	Number of Cases	Mean (Cm.)	Number of Cases	Mean (Cm.)
3 mo.	1	3.70	1	52.2	1	50.0	1	32.0	1	9.5
6 mo.	4	5.64	4	59.6	4	60.1	4	38.4	4	14.4
9 mo.	2	5.61	2	63.5	2	62.2	2	40.5	2	15.6
1 yr.	2	8.41	2	69.9	2	68.5	2	43.5	2	14.8
1½ yr.	5	8.12	4	72.8	5	70.1	5	44.0	5	15.5
2 yr.	3	9.17	3	80.3	3	78.3	3	46.6	3	15.9
2½ yr.	2	10.02	2	76.8	2	79.5	2	45.5	2	16.5
3 yr.	4	10.31	4	80.2	4	80.2	4	48.9	4	16.4
3½ yr.	3	11.50	3	86.2	3	86.3	3	49.8	3	17.1
4 yr.	6	11.01	5	85.6	6	85.7	6	49.9	6	16.6
4½ yr.	3	12.63	3	94.4	3	92.5	3	50.3	3	18.2
5 yr.	3	14.16	3	97.9	3	94.8	3	52.5	3	19.3
5½ yr.										
6 yr.	4	16.43	4	106.0	4	106.2	4	53.4	4	19.4
6½ yr.	3	15.90	3	103.7	4	103.5	4	54.5	4	20.1
7 yr.	10	17.13	10	107.9	10	107.0	10	54.6	9	20.3
7½ yr.	2	15.00	2	105.5	2	105.8	2	54.0	2	18.5
8 yr.	6	15.63	6	109.2	6	106.7	6	54.3	6	19.3
8½ yr.	2	19.90	2	117.4	2	118.0	2	57.0	2	19.8
9 yr.	7	18.83	8	116.6	8	117.2	8	56.1	8	20.9
9½ yr.	4	22.22	4	120.3	4	120.0	4	60.0	3	22.3
10 yr.	9	21.81	9	123.0	9	122.7	8	59.6	9	21.9

*Up to 3 years of age, length; 3 years and over, height.

Chart 2 shows a similar situation with regard to stature, with nearly all the points for the Madrid means below the minus two sigma curve for the Boston children.

Chart 3 indicates that there is less difference between the groups with respect to chest circumference, although there is still a consistent tendency for the means for chest circumference to be lower in the Madrid series.

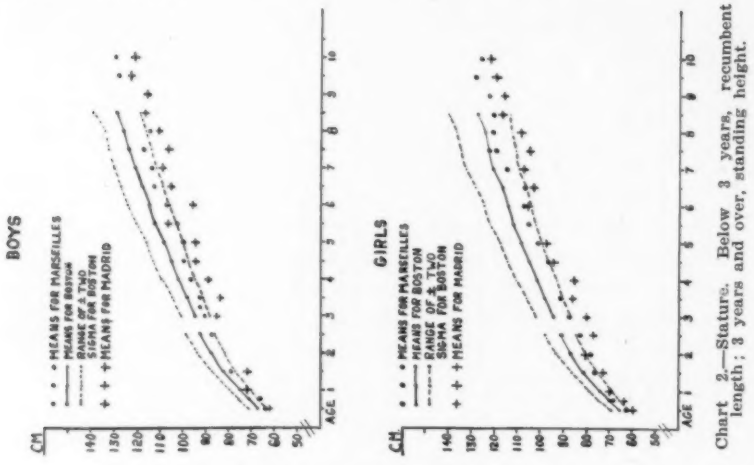

Chart 2.—Stature. Below 3 years, recumbent length; 3 years and over, standing height.

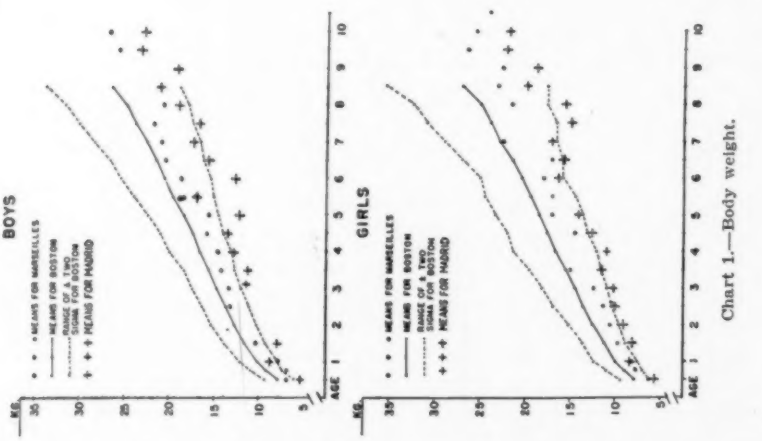

Chart 1.—Body weight.

Pelvic breadth, as plotted in Chart 4, shows much closer agreement between the Madrid and Boston series than do the other measurements, with means for the Madrid children falling on both sides of the curve for the means of the Boston children.

From these charts it appears that the Madrid children of both sexes are strikingly short and light in weight as contrasted with the Boston children, somewhat smaller in chest circumference, and about the same in breadth of pelvis. Aside from pelvic breadth, the differences are directionally the same but greater in magnitude than those found in the Marseilles children.

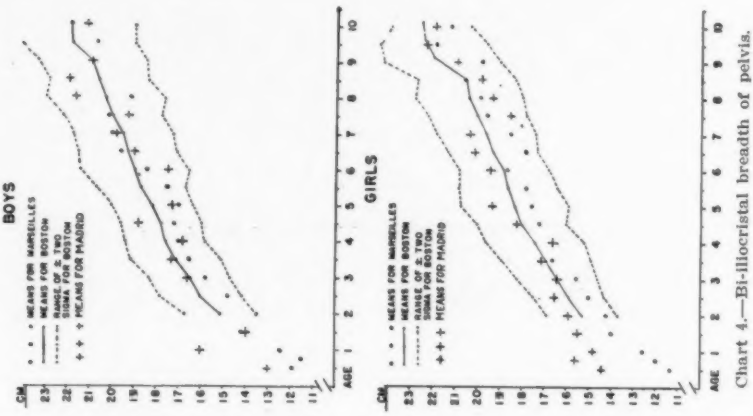

Chart 4.—Bi-iliocristal breadth of pelvis.

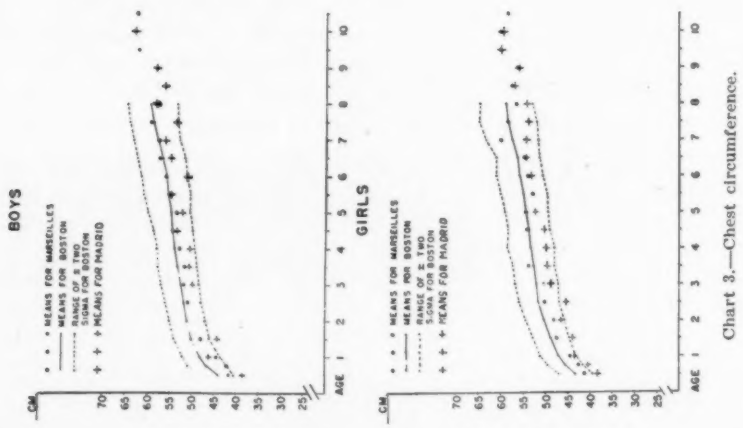

Chart 3.—Chest circumference.

Chart 5 represents an attempt to overcome the difficulties introduced by the effect which the shorter stature of the Madrid children would have on body weight. In making this chart, age has been ignored and the body weights have been grouped according to stature at 2.5 cm. intervals; the mean of each such group has been calculated and plotted. The reference curve is derived from the figures of average weight for

height for the United States as a whole, as originally published by Woodbury[4] and by Baldwin and Wood.[5] The tendency of the Madrid values to be below the American norms persists. When the per cent

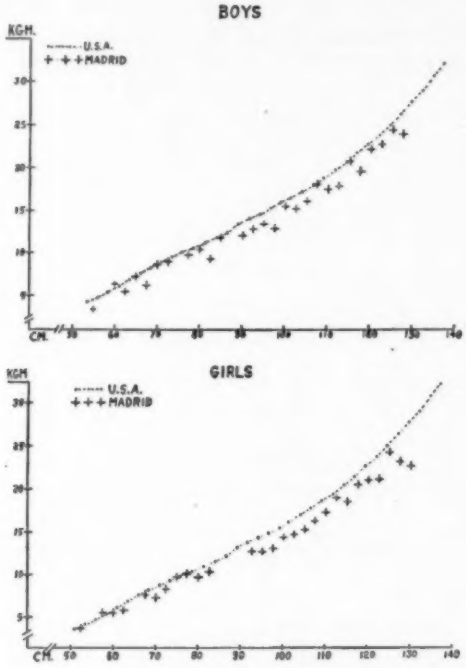

Chart 5.—Body weight for stature.

variation from standard weight for height is calculated for each child in the Madrid study, using the same American standards, the results are as follows:

	3 TO 24 MO.		2 TO 5 YEARS		6 TO 10 YEARS		TOTAL	
	BOYS	GIRLS	BOYS	GIRLS	BOYS	GIRLS	BOYS	GIRLS
Number in group	13	15	19	23	43	49	75	87
More than 7.5 per cent overweight	1	2	0	0	1	1	2	3
Between 7.5 per cent overweight and 7.5 per cent underweight	5	5	10	12	21	16	36	33
More than 7.5 per cent underweight	7	8	9	11	21	32	37	51
More than 12.5 per cent underweight	5	4	7	5	16	16	28	25

From these data it appears that a number of these children are significantly underweight for their body stature as well as for their chronologic age.

In order to consider each child from the standpoint of his position with respect to the normal distribution (according to the Boston norms), measurements for each child from 1 through 8 years of age have been given a ranking in Tables III and IV indicating the degree of deviation from the Boston norms. An entry in the column headed Below $-3\ \sigma$ indicates that the measurements fell more than three standard deviations below the mean for the Boston children of that age; an entry in the column headed m to $+1\ \sigma$ indicates that it fell between the mean and one standard deviation above the mean. The additions at the bottom of the columns in these tables show, in contrast to the 5 per cent who would be expected to fall more than two standard deviations below the mean, the following figures:

	BOYS	GIRLS
Weight	55%	68%
Stature	68%	70%
Chest circumference	27%	41%

In contrast to the 18 per cent who would be expected to fall more than one standard deviation below the mean, the figures are as follows:

	BOYS	GIRLS
Weight	83%	87%
Stature	89%	93%
Chest circumference	45%	61%

The ranks for pelvic breadth indicate somewhat more variability than would be anticipated, with the measurements for the girls tending to be slightly higher than would be expected.

Measurements From Roentgenograms.—Tables V and VI present the means for linear measurements obtained from x-ray films of the right leg, taken and measured according to a standard technique which has been described in detail elsewhere.[3] Charts 6 to 9 inclusive give the means of these measurements plotted against the means and ranges of the same measurements taken on the Boston group and the means for the Marseilles group. Tables VII and VIII indicate the rankings of these measurements for each child with respect to the distribution according to the Boston norms in a manner identical to the rankings of the body measurements in Tables III and IV.

Certain impressions can be derived from these data. The shaft of the tibia (Chart 6) appears to be consistently much shorter in the Madrid children, in keeping with their smaller stature. The breadth of calf (Chart 7) is also consistently smaller in the Madrid group, in contrast to the Marseilles children who were at or near the Boston mean in all the breadth measurements. Although the values for both breadth of calf muscle (Chart 8) and breadth of skin and subcutaneous tissue (Chart 9) are usually much lower in the Madrid children, smaller

TABLE III

RANKS FOR BODY MEASUREMENTS FOR BOYS
MADRID CHILDREN COMPARED WITH BOSTON NORMS

AGE	WEIGHT					LENGTH OR HEIGHT					CHEST CIRCUMFERENCE					PELVIC BREADTH					
	Below -3σ	-2σ to -3σ	-1σ to -2σ	m to -1σ	m to $+1\sigma$	Below -3σ	-2σ to -3σ	-1σ to -2σ	m to -1σ	m to $+1\sigma$	-2σ to -3σ	-1σ to -2σ	m to -1σ	m to $+1\sigma$	$+1\sigma$ to $+2\sigma$	-2σ to -3σ	-1σ to -2σ	m to -1σ	m to $+1\sigma$	$+1\sigma$ to $+2\sigma$	$+2\sigma$ to $+3\sigma$
3 mo.					1					1			1								
6 mo.	2	1		1		1	1	1	1		3			1							
9 mo.		1					1				1										
1 yr.		2	1	2				3	2		1		2	2							
1½ yr.	1			1		1	1				2										
3 yr.	2	1		1		3				1		3	1			1		1	1		1
3½ yr.	1	1				1	1					1	1					1		1	
4 yr.	1	1	2			1	3				1	1	2			1	2			1	
4½ yr.	1	1		1		2		1			1			1	1			1	1		1
5 yr.	2	1				2	1				1	1	1				1	2			
5½ yr.			2	1				2	1				2								1
6 yr.	2	1				2	1				2		1			1		2			
6½ yr.	1	3	4			3	3	2			1	1	3	2			2	3	2	1	
7 yr.	1		3			1	1	2			1		2		1			1	2	1	
7½ yr.		3	1	1		3	1	1			1	2	1	1		1		1	3		
8 yr.		1	3	1		3	2					1	2	2				1	2		2
Totals	14	17	16	9	1	23	16	12	4	2	15	10	19	9	2	4	5	13	11	4	5
Grand Total			57					57					55					42			
Per cent	25	30	28	16	2	40	28	21	7	4	27	18	35	16	4	10	12	31	26	10	12

TABLE IV

RANKS FOR BODY MEASUREMENTS FOR GIRLS

MADRID CHILDREN COMPARED WITH BOSTON NORMS

AGE	WEIGHT				LENGTH OR HEIGHT					CHEST CIRCUMFERENCE					PELVIC BREADTH					
	Below -3σ	-2σ to -3σ	-1σ to -2σ	m to -1σ	Below -3σ	-2σ to -3σ	-1σ to -2σ	m to -1σ	m to $+1\sigma$	-2σ to -3σ	-1σ to -2σ	m to -1σ	m to $+1\sigma$	$+1\sigma$ to $+2\sigma$	-2σ to -3σ	-1σ to -2σ	m to -1σ	m to $+1\sigma$	$+1\sigma$ to $+2\sigma$	$+2\sigma$ to $+3\sigma$
3 mo.	1				1					1										
6 mo.	1	2	1		2		2			3	1									
9 mo.	1	1				2				2										
1 yr.			1	1		1	1			1	1									
1½ yr.	3	1		1	1	2	1			4		1								
2 yr.		2	1			1	2			1	1		1			1		1		1
2½ yr.		1	1		2					1			1				1		1	
3 yr.		4			4					1	1	2					3		2	
3½ yr.		2		1	2			1		1	1			1			1	1	1	
4 yr.	2	2	1		3	1	1			2		4			1	1	3	1		
4½ yr.		3				2	1			1	1	1					1	2		
5 yr.		1	2		1	1	1				1	2							2	1
6 yr.	1	1		2	1		1	2		2			2			1		1	1	1
6½ yr.	1	1		1	1	1	1				2	1	1				2	1		1
7 yr.	2	2	4	2	3	4	2	1		2	3	3	2			1	4	1	1	2
7½ yr.		2			1	1				1		1					1	1		
8 yr.	2	3	1		2	3	1			3	1	1	1			2	3	1		
Totals	14	28	12	8	24	19	14	4		26	13	16	8	1	1	6	19	10	8	6
Grand Total	62				61					64					50					
Per cent	23	45	19	13	39	31	23	7		41	20	25	12	2	2	12	38	20	16	12

measurements for the muscle appear to be a more important and consistent factor in affecting the total calf breadth than those for skin and subcutaneous tissue. The small number of children included in each age group precludes making any inferences regarding age and sex predilection.

TABLE V

MEANS FOR THE LINEAR MEASUREMENTS FROM ROENTGENOGRAMS OF BOYS

AGE	LENGTH OF TIBIA		BREADTH OF HEAD OF TIBIA		BREADTH OF CALF		BREADTH OF MUSCLE		BREADTH OF SKIN AND SUBCUTANEOUS TISSUE	
	NUMBER OF CASES	MEAN (CM.)	NUMBER OF CASES	MEAN (CM.)	NUMBER OF CASES	MEAN (CM.)	NUMBER OF CASES	MEAN (CM.)	NUMBER OF CASES	MEAN (CM.)
6 mo.	3	8.3	2	2.5	2	5.4	2	3.9	2	1.6
		9.3		*2.6*		*5.9*		*4.0*		*1.9*
1 yr.	2	10.6	2	3.0	2	5.5	2	4.2	2	1.2
		11.1		*3.0*		*6.6*		*4.7*		*1.9*
1½ yr.	2	10.4	2	2.8	2	5.0	2	3.8	2	1.1
		12.6		*3.4*		*6.8*		*5.1*		*1.7*
2 yr.										
2½ yr.										
3 yr.	3	13.3	3	3.6	3	6.4	3	5.3	3	1.4
		16.4		*4.2*		*7.2*		*5.8*		*1.4*
3½ yr.	2	14.1	2	3.5	2	6.4	2	5.0	2	1.4
		17.4		*4.4*		*7.4*		*6.1*		*1.3*
4 yr.	2	14.0	2	3.6	2	6.6	2	5.6	2	1.0
		18.5		*4.5*		*7.5*		*6.2*		*1.3*
4½ yr.	3	15.9	3	4.1	3	6.4	3	5.7	3	0.8
		19.5		*4.6*		*7.7*		*6.5*		*1.2*
5 yr.	1	15.7	1	4.0	1	5.6	1	5.1	1	0.5
		20.2		*4.7*		*7.7*		*6.6*		*1.2*
5½ yr.	1	19.4	1	4.2	1	6.6	1	5.1	1	1.5
		21.2		*4.8*		*8.0*		*6.8*		*1.2*
6 yr.	3	17.0	3	4.2	3	6.3	3	5.5	3	0.7
		22.0		*4.9*		*8.1*		*7.0*		*1.1*
6½ yr.	6	18.7	6	4.6	6	6.9	6	6.2	6	0.7
		23.0		*5.1*		*8.2*		*7.1*		*1.1*
7 yr.	4	19.7	4	4.7	4	7.5	4	6.8	4	0.7
		23.5		*5.2*		*8.2*		*7.2*		*1.1*
7½ yr.	3	19.7	3	4.7	3	7.8	3	7.0	3	0.8
8 yr.	2	20.3	2	4.8	2	7.3	2	6.8	2	0.6
8½ yr.	1	23.7	1	5.0	1	8.4	1	7.4	1	1.0
9 yr.	5	22.0	5	4.8	5	6.8	5	6.2	5	0.6

Figures in italics give the corresponding means for the Boston series.

Developmental Status.—The stage of osseous development, as evidenced in roentgenograms of the hand and wrist, furnished a basis for comparing the levels of anatomical development attained by the Madrid children at each age with American norms. The Atlas prepared by Todd and others[6] and the chart prepared by Vogt and Vickers[7] were used in making this comparison. To each x-ray film was assigned the osseous age of the standard picture to which it most nearly corresponded or an age midway between two standard films when neither corresponded closely, when averaging all the features to be taken into

account. The age groups were restricted to a deviation of six weeks from the birthday in children below 2 years of age and a deviation of three months in those older.

Table IX presents the variation of osseous age from chronologic age for each of the ninety-eight children so studied. It shows that whereas very few of them showed advancement of more than six months in osseous development, from one-half to two-thirds showed retardation of more than six months and in many of these the retardation was severe in degree.

TABLE VI

MEANS FOR THE LINEAR MEASUREMENTS FROM ROENTGENOGRAMS OF GIRLS

AGE	LENGTH OF TIBIA		BREADTH OF HEAD OF TIBIA		BREADTH OF CALF		BREADTH OF MUSCLE		BREADTH OF SKIN AND SUBCUTANEOUS TISSUE	
	NUMBER OF CASES	MEAN (CM.)	NUMBER OF CASES	MEAN (CM.)	NUMBER OF CASES	MEAN (CM.)	NUMBER OF CASES	MEAN (CM.)	NUMBER OF CASES	MEAN (CM.)
6 mo.	3	8.4	3	2.2	3	4.7	3	3.3	3	1.4
		9.2		*2.5*		*5.8*		*3.8*		*1.9*
1 yr.	3	10.2	3	2.7	3	6.0	2	4.0	2	2.2
		11.1		*2.9*		*6.5*		*4.5*		*1.9*
1½ yr.	2	9.8	2	2.4	2	5.0	1	4.2	1	1.6
		12.8		*3.4*		*6.7*		*5.0*		*1.8*
2 yr.										
2½ yr.	1	12.2	1	3.3	1	6.6				
		15.5		*3.9*		*7.2*				
3 yr.	3	12.5	3	3.4	3	5.6	3	4.5	3	1.1
		16.3		*4.1*		*7.3*		*5.8*		*1.6*
3½ yr.	3	14.4	3	3.7	3	6.2	3	5.0	3	1.2
		17.6		*4.2*		*7.6*		*6.1*		*1.5*
4 yr.	5	14.1	5	3.5	5	6.5	5	5.4	5	1.1
		18.8		*4.3*		*7.8*		*6.3*		*1.5*
4½ yr.	1	16.1	1	3.7	1	6.5	1	5.3	1	1.2
		19.7		*4.4*		*7.9*		*6.5*		*1.4*
5 yr.	2	16.8	2	4.2	2	6.8	2	5.8	2	1.1
		20.6		*4.5*		*8.0*		*6.6*		*1.4*
5½ yr.										
6 yr.	2	21.1	1	4.2	1	7.2	1	5.9	1	1.3
		22.4		*4.7*		*8.2*		*6.8*		*1.4*
6½ yr.	2	18.8	2	4.4	2	7.9	2	6.9	2	1.0
		23.2		*4.8*		*8.4*		*7.1*		*1.3*
7 yr.	5	19.3	4	4.5	4	7.4	4	6.5	4	0.9
		24.1		*4.9*		*8.6*		*7.2*		*1.4*
7½ yr.	2	19.8	2	4.2	2	6.6	2	5.8	2	0.8
8 yr.	2	21.2	2	4.4	2	7.3	2	6.4	2	0.8
8½ yr.	1	22.5	1	4.8	1	8.0	1	6.9	1	1.1
9 yr.	6	22.3	5	4.8	6	7.8	6	6.8	6	1.0
9½ yr.	4	23.3	4	5.0	4	8.0	4	6.6	4	1.4

Figures in italics give the corresponding means for the Boston series.

There was abundant evidence of faulty bone structure or disturbances of bone growth in the roentgenograms of the wrist and leg. Bands of differing densities, dense lines of interrupted growth, irregular bone trabeculations, widening of the growth zone, or other evidences of faulty

TABLE VII

RANKS FOR SELECTED MEASUREMENTS FROM ROENTGENOGRAMS OF BOYS
MADRID CHILDREN RELATED TO BOSTON NORMS

AGE	LENGTH OF TIBIA					BREADTH OF MUSCLE					BREADTH OF SKIN AND SUBCUTANEOUS TISSUE				
	Below -3σ	-2σ to -3σ	-1σ to -2σ	m to -1σ	m to $+1\sigma$	-2σ to -3σ	-1σ to -2σ	m to -1σ	m to $+1\sigma$	$+1\sigma$ to $+2\sigma$	-2σ to -3σ	-1σ to -2σ	m to -1σ	m to $+1\sigma$	$+1\sigma$ to $+2\sigma$
6 mo.	1			2				1		1		1		1	
1 yr.		1			1		1	1			1	1			
1½ yr.	1	1				1	1				1	1			
3 yr.	2	1					2	1					1	2	
3½ yr.	1	1				1	1							2	
4 yr.	2					1			1			1	1		
4½ yr.	2	1					3				2		1		
5 yr.	1					1					1				
5½ yr.			1			1									1
6 yr.	2	1				3						2		1	
6½ yr.	4	2				1	3	1	1			6			
7 yr.	1	2	1			1	1		2			2	2		
Total	17	10	2	2	1	10	12	4	4	1	5	14	5	6	1
Grand total	32					31					31				
Per cent	53	31	6	6	3	32	39	13	13	3	16	45	16	19	3

TABLE VIII

RANKS FOR SELECTED MEASUREMENTS FROM ROENTGENOGRAMS OF GIRLS

MADRID CHILDREN RELATED TO BOSTON NORMS

AGE	LENGTH OF TIBIA					BREADTH OF MUSCLE					BREADTH OF SKIN AND SUBCUTANEOUS TISSUE				
	Below -3σ	-2σ to -3σ	-1σ to -2σ	m to -1σ	m to $+1\sigma$	-2σ to -3σ	-1σ to -2σ	m to -1σ	m to $+1\sigma$	$+1\sigma$ to $+2\sigma$	-2σ to -3σ	-1σ to -2σ	m to -1σ	m to $+1\sigma$	$+1\sigma$ to $+2\sigma$
6 mo.	1		1	1		1		2				2	1		
1 yr.		1	1	1		1			1					1	1
1½ yr.	2						1						1		
2½ yr.	1														
3 yr.		3				3					1	2			
3½ yr.	2		1			2			1		1		2		
4 yr.	3	2				2	2	1			3		1	1	
4½ yr.		1				1							1		
5 yr.	1	1				1		1				2			
6 yr.		1			1		1						1		
6½ yr.		2						1	1			2			
7 yr.	3		1	1		2			2		1	3			
Total	13	11	4	3	1	13	4	5	5		6	11	7	2	1
Grand total	32					27					27				
Per cent	41	34	12	9	3	48	15	18	18		22	41	26	7	4

or irregular osseous development were present in nearly all the films of children up to 6 years of age. Thereafter the only evidence of faulty calcification recognizable was thick lines of increased density persisting well above the growth zones, seen in about one-half of the films. Two

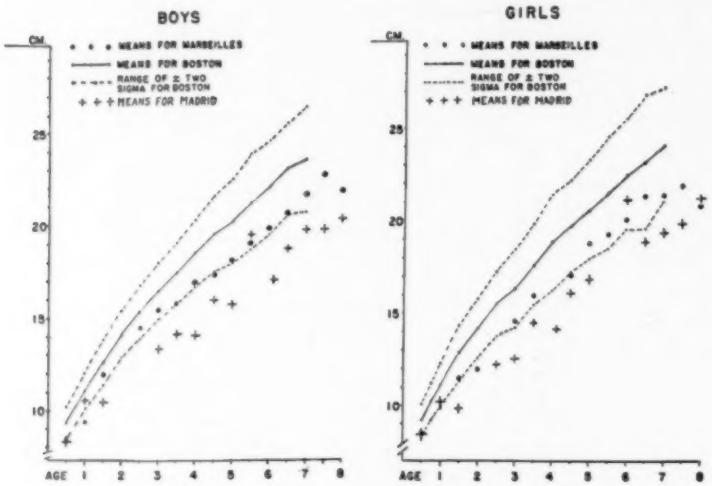

Chart 6.—Length of tibial shaft by x-ray.

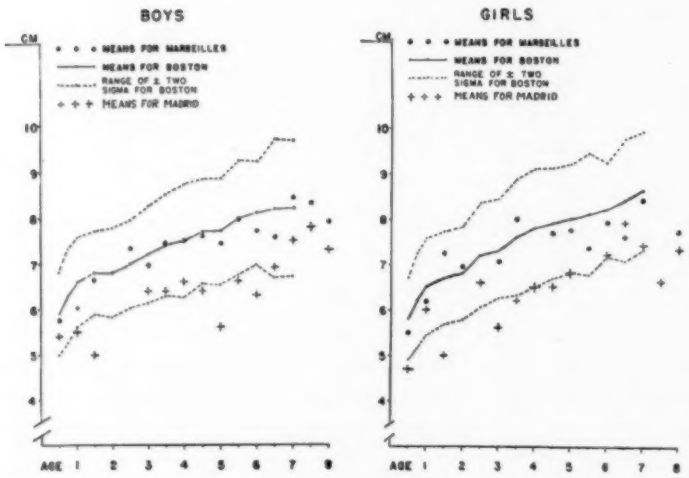

Chart 7.—Total breadth of calf by x-ray.

cases of active rickets were diagnosed by x-ray among twenty children under the age of 2 years on whom satisfactory films were obtained. In addition, one child of 3 years of age showed definite roentgenographic

evidence of incompletely healed rickets. In considering the incidence of rickets, it should be recalled that this study was carried out during the summer months and that there is circumstantial evidence that these children were not growing.

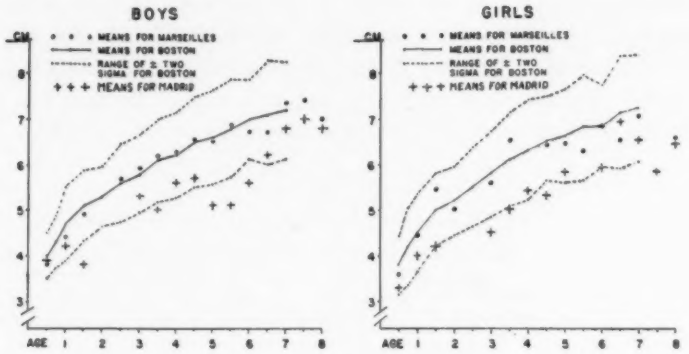

Chart 8.—Breadth of calf muscle by x-ray.

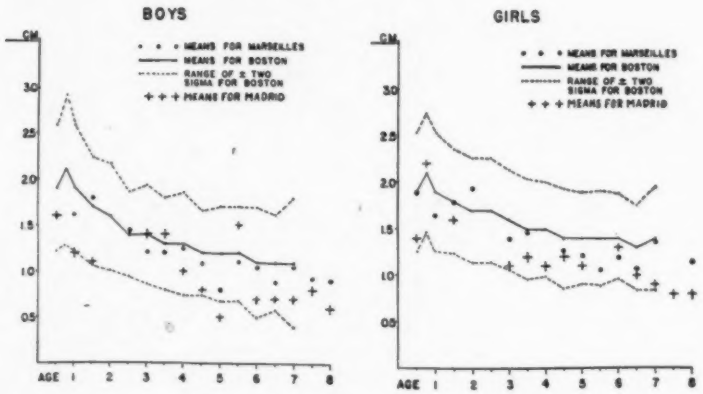

Chart 9.—Breadth of two thicknesses of skin and subcutaneous tissue in calf by x-ray.

In the course of the clinical examination of these children, the incidence of poorly developed or relaxed abdominal musculature was as follows: under 2 years of age, four out of twenty-nine (14 per cent); 2 to 5 years inclusive, twenty-one out of forty-three (49 per cent); 6 to 12 years inclusive, twenty-nine out of 115 (25 per cent).

CONCLUSIONS

A group of children from the lower economic class in Madrid, known to be subsisting on a diet inadequate in several respects at the time of the study, shows a number of differences when compared with a simi-

larly studied group of Boston children who enjoyed regular health supervision and dietary instruction. They are strikingly shorter in stature and somewhat smaller in chest circumference but about the same in pelvic breadth. As a group, they are underweight, when both their age and shorter stature are taken into account. Linear measurements from roentgenograms suggest that this is associated with smaller bulk of muscle as well as subcutaneous tissue. The Madrid children show essentially the same differences, though less marked in degree, when compared with a sample of Marseilles children similarly studied.

TABLE IX

OSSEOUS DEVELOPMENT OF HANDS AND WRISTS OF MADRID CHILDREN BY X-RAY

	VARIATION OF OSSEOUS AGE FROM CHRONOLOGIC AGE IN MONTHS																				
	ADVANCED						RETARDED														
	27	21	15	9	6	3	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45
ACCORDING TO TODD'S STANDARDS																						
Boys																						
3 to 24 mo.				1			1	4	2													
2 to 7 yr.	1				1	1		1	1	5	1	3	1	3		5	2			1		1
7½ to 9½ yr.				1		1						1	1	2	1	2		1			1	1
Girls																						
3 to 24 mo.							2	3	1	2	1	1										
2 to 7 yr.			1	2	1	2		1	1	1	2	4	1	4	2	1			1			
7½ to 9½ yr.						2		1				4	1	3	2	2			2			
ACCORDING TO STANDARDS OF VOGT AND VICKERS																						
Boys																						
3 to 24 mo.				1			1	6														
2 to 7 yr.	1				1		1	2	2	2	4		3	2	1	3	2	1		1		1
Girls																						
3 to 24 mo.						2	2	3	1	1	1											
2 to 7 yr.	1			1	2	1	1	1	2		4	2	5	3		1						

	STANDARDS OF TODD		STANDARDS OF VOGT AND VICKERS	
	BOYS	GIRLS	BOYS	GIRLS
Number of children studied	47	51	35	34
Number advanced more than six months	3 (6%)	3 (6%)	2 (6%)	2 (6%)
Number retarded more than six months	32 (68%)	34 (67%)	20 (57%)	17 (50%)
Average retardation in months of those over six months retarded	23.0 mo.	19.6 mo.	22.2 mo.	16.4 mo.

Roentgenographic evidence of retarded osseous development and interference with normal bone growth in the Madrid children suggest that these differences may be due to environmental as well as racial factors. Data on the growth of these children under known dietary and health conditions is now being collected and should yield more conclusive information on this point.

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DARK ADAPTATION OF CHILDREN IN RELATION TO DIETARY LEVELS OF VITAMIN A

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AFTER an extensive study of the validity of the biophotometer test as an index of nutritional status with respect to vitamin A, Steininger and Roberts[1] reported that although there appeared to be some relationship between biophotometer readings and vitamin A nutrition, the relation was "not close enough to warrant the use of the test as a means of diagnosing subclinical vitamin A deficiency." Shortly before this study was completed, another instrument for testing visual adaptation (the adaptometer) was designed by Hecht and Shlaer.[2] Since in this instrument some of the less desirable features of the biophotometer appeared to have been eliminated, it seemed worth while to determine the reliability and validity of tests made by this instrument in a study similar to that in which the biophotometer was used.

Investigators from several laboratories (Hecht and Mandelbaum[3, 4] Wald and his associates,[5] and Booher and her associates[6] have reported that when subjects are put on depletion diets their readings on the adaptometer become progressively higher (that is, they have poorer dark adaptation) as they continue to ingest diets extremely low in vitamin A. These readings moreover eventually fall to a normal level when the diets are supplemented with vitamin A or carotene. Such results indicate that the adaptometer test would be useful in identifying subjects markedly depleted of vitamin A. More recently, Steven and Wald[7] have suggested that a deficiency may be measured more reliably by a vitamin A labile threshold than by comparison of readings with a "normal range," which has been the customary procedure. Whether or not the test, as interpreted by either method, is of practical value in detecting subclinical vitamin A deficiency in its early stages, such as might be found in public school populations, has, however, not yet been established. Lewis and Haig,[8] using a modified form of the adaptometer, studied the dark adaptation of a large group of children in New York City, the majority of whom came from poor homes, and found the adaptometer readings to be normal in all but one child. Since no changes were observed in the rod plateaus of eight normal children when large supplements of vitamin A were given over a period of six weeks, the authors conclude that, as judged by dark adaptation, vitamin A deficiency is an uncommon disorder in New York City children. It is

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obvious that these results might also be interpreted to mean that the test, as used in their study, does not adequately measure early stages of vitamin A deficiency.

The present study makes a further contribution to the problem of the validity of the test and its usefulness in diagnosing subnutrition for vitamin A in practical school situations. It reports the correlation of adaptometer readings and dietary studies, the effect of vitamin A supplements on dark adaptation, and a comparison of adaptometer readings of groups of children from different socio-economic levels.

SELECTION OF SUBJECTS

The subjects used in this study,* having widely different dietary histories, may be classed into three groups. Group A consisted of 100 children between the ages of 9 and 13 years from a grade school in one of the poorest sections of the city. Preliminary observation indicated that the diets of the majority of these children were low in vitamin A, and subsequent dietary studies showed this to be the case. Group B was composed of forty-five children 8 to 16 years of age who were living in a girls' school in which the diet was known to be fairly adequate. Group C consisted of twenty-three children 8 to 12 years of age from the laboratory school of the University of Chicago. The members of this group were in excellent physical condition and came from comfortable and well-to-do homes where there should be no shortage of vitamin A.

METHODS

Standardization and Reliability of the Test Procedure.—The test procedure used was that described by Hecht and his associates.[2, 3] Minor details of the procedure were standardized by combining directions which had been formulated independently by three different operators. The adaptation of both the cones and rods was followed, and the curves obtained were very similar to those published by the Columbia workers. In compiling results only rod thresholds† have been used since they show the greatest change when a subject is depleted and, therefore, should be the most indicative of the subject's status. In order to rule out the possibility that the gelatin wedge of the adaptometer had gradually deteriorated during the course of the study, as suggested by Hunt and Palmer,[9] the same group of college women were tested when the study was well under way and again when the study was completed. The rod plateaus of the majority of the subjects agreed with those of the original test within 0.2 log unit and the greatest difference found was 0.4 log unit. It seemed safe, therefore, to assume that the results as herein reported were not influenced by wedge deterioration.

*Grateful acknowledgment is given to Miss Helen Kull, principal, and to the teachers of the Froebel School; to Miss Ruby Badger, superintendent of the Park Ridge School for girls, and to Mr. Harry Gillet, principal of the University Elementary School, for their cooperation which made the study possible.

†The term rod threshold, as used in this study, refers to the final threshold or the rod plateau.

The reliability of the instrument when the standardized test was used was determined by successive tests on the same subjects by different as well as the same operators. It was found that the day-to-day variation was, for the most part, within 0.3 of a log unit (the amount reported in normal individuals by Hecht and Mandelbaum[3]). Since both adults and children showed virtually the same variation, the test seemed to be reliable when used on children. Furthermore, when a comparison of the readings of the first and second tests of a group of forty-six children showed the second tests to be poorer than those of the first in sixteen subjects, better in twenty-three, and the same in seven, it seemed that there was no so-called "learning factor" on this instrument. Therefore, in this study the first test was considered as dependable as the second.

DIETARY STUDIES

Since the purpose of the study was to determine the relation between the test and vitamin A status, effort was made to obtain as accurate estimates as possible of the customary vitamin A intakes of the subjects.

In the group of 100 children in the poorer section which was studied most intensively (Group A), daily diet records were compared with information obtained from repeated personal interviews. The variation found was never sufficient to change the level of vitamin A intake markedly. Additional information concerning the intake of the group was gained by examining the menus and the amounts of foods served in the school lunchroom for a period of several months and by having the few children who were taking vitamin concentrates bring the containers for inspection. While it is obvious that this type of study is not quantitatively accurate, it does give as true a picture of the dietary habits of a group as it is possible to obtain without actually weighing the amounts of food consumed.

For the forty-five subjects residing in a girls' school (Group B) it was possible to secure a more exact record of food intakes. Each girl kept an individual record of the number of servings of each food consumed for a period of two weeks. Average servings of foods containing appreciable amounts of vitamin A were weighed, and these weights were used to calculate the food intake of the individual subjects. The average amounts of vitamin A in the daily intakes of the individual members of both groups were calculated, using the values of Daniel and Munsell.*[10]

Vitamin A Intakes of the Subjects.—When the vitamin A in the diets of the subjects was computed by the methods described, the intakes were found to vary greatly (Table I). In the poorer group (A), 41 per cent of the 100 children were receiving on the average less than 40 international units per kilogram daily, and 11 per cent had even less than 20 international units per kilogram. The forty-five girls in Group

*All values expressed as Sherman units were converted to international units by dividing by 2. This factor was used, since it is the one most generally accepted. It is recognized, however, that the exact conversion factor for changing Sherman units into international units has not been definitely established.

B were on a uniformly higher level of intake. No subject had less than 20 and only 11 per cent less than 40 international units per kilogram. For the twenty-three children from the University elementary school, no dietary study was made, but it was obvious that the excellent physical condition of the group was the result of good diets as well as excellent living conditions and proper medical care. Over one-half of the children of the group reported that they had taken additional vitamin A in some form through the winter months. It is seen that the three groups thus represented three different levels of vitamin A intake: low, medium, and relatively high.

TABLE I

AVERAGE DAILY VITAMIN A INTAKES OF GROUPS A AND B

DAILY INTAKE OF VITAMIN A (I.U./KG.)	GROUP A			GROUP B		
	NO.	PER CENT		NO.	PER CENT	
0 to 19	11	11	41	--	--	
20 to 39	30	30		5	11.1	
40 to 59	20	20		11	24.4	
60 to 79	14	14		10	22.2	
80 to 99	7	7	39	12	26.7	64.5
100 or more	18	18		7	15.6	

VALIDITY OF THE ADAPTOMETER TEST

An attempt was made to determine the validity of the test as an index of the nutritional status of a subject in respect to vitamin A by three approaches: (1) A comparison was made of the mean adaptometer readings of subjects from low, medium, and high socio-economics groups (Groups A, B, and C); (2) the amount of vitamin A in the individual diets of 145 children was correlated with their adaptometer readings; (3) the effect of supplementation on the adaptometer readings of subjects known to have a low vitamin A intake was studied and the results compared with those of a matched group which were not given the supplement.

Mean Adaptometer Readings of Groups in Relation to Socio-Economic Status.—If the adaptometer test measures vitamin A stores accurately enough to be of practical use in assessing nutritional status, there should be a significant difference between the adaptometer readings of groups having poor, fair, and good dietary histories, such as the three groups described above. In spite of what seemed to be wide differences in the vitamin A intakes of these three groups, however, no such difference in their dark adaptation was observed. The mean rod plateau readings of the three groups were found to be almost identical; namely, 3.00, 3.10, and 3.04 log units for Groups A, B, and C, respectively. Moreover, when the groups were classified into "normal" and "subnormal" zones, according to the limits suggested by Hecht (normal zone 2.5 to 3.5 log units), the distribution was again almost identical. The percentage of children in the subnormal zone was 14 for Group A, 15

for Group B and 13 for Group C. The remaining subjects in each group were classed as having normal readings. There is thus seen to be no detectable difference in the mean adaptometer readings of these three groups of children, even though their intakes of vitamin A varied widely.

Correlation of Vitamin A Intakes of Individuals With Their Adaptometer Readings.—Mean intakes of groups, however, may be deceiving due to wide variation in individuals within the various groups. A more crucial approach is to determine the degree of correlation between the vitamin A in the diets of individuals and their dark adaptation readings.

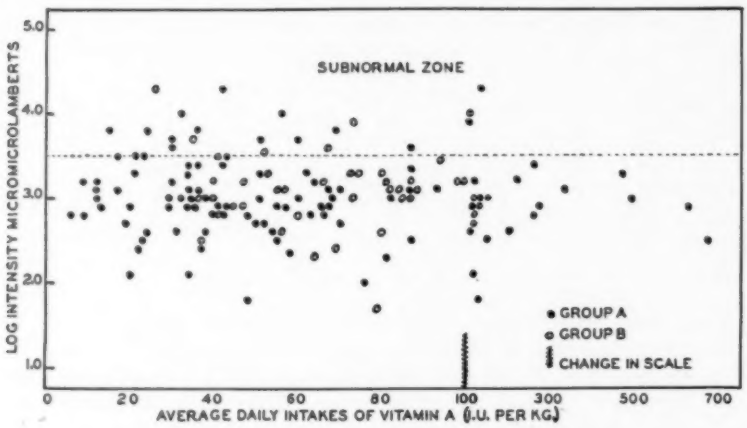

Fig. 1.—Rod plateau readings and vitamin A intakes.

In the present study such data were available for the 145 children in the two major groups. The results of this type of evaluation are best seen in Fig. 1, in which vitamin A intakes are plotted against rod thresholds. If there were a close correlation between dark adaptation and vitamin A in the diet, it would be evidenced by a definite trend downward of the dots from left to right. Even though the dietary records were admittedly only roughly quantitative, if a real relationship existed there would be an indication of such a trend. It is obvious that such is not the case. Instead there is a wide spread in the vitamin A intake at any given rod threshold level and similarly a wide range in rod threshold readings at a given level of vitamin A. At the level of intakes represented by these subjects, therefore, there appears to be no relation between the vitamin A in the diets and the readings on the adaptometer. It is interesting to note, however, that after the intakes reach 150 international units per kilogram there are no cases of subnormal dark adaptation and that there are only three cases on intakes of over 90 international units per kilogram.

The Effect of Vitamin A Supplementation on Adaptometer Readings.—The third approach to the validity of the test was to determine the effect of vitamin A supplements on adaptometer readings. As already pointed out, 86 per cent of the children in this study fell in the normal zone, according to Hecht's classification based on adults. Since earlier studies on the biophotometer had shown that children have somewhat better dark adaptation than adults, the possibility that the readings of the children in this study might improve with continued vitamin A supplements, especially those with poorest readings, was not overlooked. The children in Group A were chosen to receive this supplementation because of the poorer quality of their diets.

Fifty pairs of children were matched as carefully as possible as to rod threshold, dietary history, age, weight, and sex. One of each pair was then given approximately 25,000 international units of vitamin A* each school day for a period of nine weeks. The other received no supplementation and served as a control. After two weeks of supplementation a second test was made of both control and experimental groups, and at the end of nine weeks the third and final tests† were made. In order to determine whether larger supplements might have a greater effect in lowering rod thresholds, fourteen of the experimental children were given approximately 78,000 international units of vitamin A daily during the last two weeks of the study. The effect of the supplement was judged by comparing the mean rod thresholds, the labile thresholds, and the relative progress of the experimental and control groups.

Mean Rod Thresholds.—The mean rod thresholds for experimental and control groups on each of the tests are shown in Fig. 2, *A*. A comparison of the readings for the two groups reveals that although there is no change at the end of two weeks, by the end of the nine weeks the supplemented group has improved slightly, 0.06 log unit, while the control group is poorer by 0.13 log unit, thus making a difference of 0.19 log unit between the groups. This difference, though small, is found to be statistically significant, for such a difference would arise by chance only 67 times in 10,000. Even though statistically significant, however, it must be recognized that the difference is not great enough to be of practical significance, since it is less than the normal day-to-day variation in the test itself.

Since this evaluation was made on the whole group, however, it was recognized that significant improvement in some of the poorest cases might have been masked by inclusion of children who had normal adaptation at the outset. To check on this possibility, the fifty matched pairs were arranged into groups of seven pairs each, ranging from

*Oleum percomorphum capsules were furnished by courtesy of Mead Johnson & Co. The capsules were swallowed in the presence of an observer.

†Since rod thresholds seemed to be the most reliable reading, these only were determined in the final tests. A group of children were taken into the dark room and one by one were subjected to the bleaching light. They then remained in the dark room for a period of thirty minutes, after which readings were taken until the rod thresholds were established.

those with "best" original rod plateau readings to the lowest seven pairs who started with readings in the subnormal zone, and the means for the several groups were compared. The results are shown in Fig. 2, *B* to *H*. It is noted that in the best seven pairs the trend for both control and experimental subjects is toward higher readings with no difference between the groups. In all other comparisons there is a noticeable difference, and in all cases but one it is in favor of the experimental subjects. This difference is most pronounced, moreover, in the seven pairs whose readings were above 3.5 at the outset (Fig. 2, *H*). In this case the experimental group made an average drop of 0.6 log unit over the nine-week period, while the control group decreased only 0.1 log unit. It is apparent, therefore, that the subjects with highest original readings show the greatest response to vitamin A supplementation.

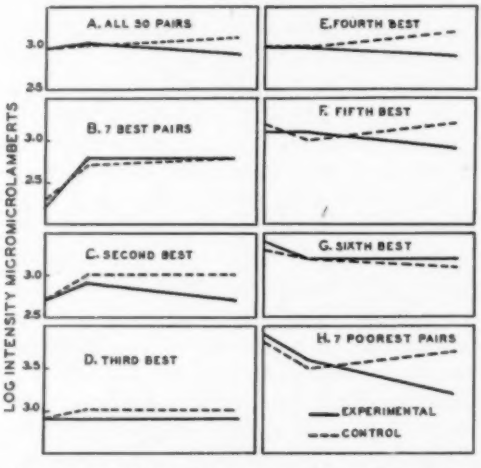

Fig. 2.—Mean rod plateau readings of experimental and control subjects arranged in groups of seven pairs from best to poorest.

Labile Thresholds.—When the data were analyzed, as suggested by Steven and Wald,[7] it was found that after two weeks of supplementation (the period suggested by these authors), ten children in the experimental group had vitamin A labile thresholds (lowered by at least 0.3 log unit after supplementation). These ten children included all but one of the experimental subjects whose original rod thresholds were over 3.5 log units, and in addition four whose original rod thresholds ranged from 2.9 to 3.5 (Table II). After nine weeks of supplementation, the thresholds of sixteen children were found to be vitamin A labile. Although a larger number of children were classed as deficient by this method than by comparison of rod thresholds with a normal range, the fact that the number showing vitamin A labile thresh-

olds after nine weeks' supplementation was larger than that after two weeks, raises the question as to how long the supplementation should be continued before it is concluded that a given subject has a threshold which is stable to vitamin A. Furthermore, analysis of the thresholds of the control subjects at the end of two weeks showed more labile thresholds in that group than in the experimental group, in spite of the fact that they had received no additional vitamin A. Therefore, if this type of test is used, it cannot be concluded with any certainty that all changes in thresholds are due solely to vitamin A supplementation unless conditions are controlled more rigidly than is possible in school situations.

TABLE II

NUMBER OF SUBJECTS IN GROUP A SHOWING LABILE THRESHOLDS

ORIGINAL ROD THRESHOLD	EXPERIMENTAL GROUP			CONTROL GROUP		
	NUMBER OF CHILDREN	VITAMIN A LABILE THRESHOLDS AFTER SUPPLEMENTATION		NUMBER OF CHILDREN	LABILE THRESHOLDS WITHOUT SUPPLEMENTATION	
		FOR TWO WEEKS	FOR NINE WEEKS		AFTER TWO-WEEK PERIOD	AFTER NINE-WEEK PERIOD
3.6 to 4.3	7	6	7	7	3	2
2.9 to 3.5	26	4	9	27	8	5
1.8 to 2.8	17	0	0	16	0	2
Total	50	10	16	50	11	9

Relative Progress of Partners in Matched Pairs.—As a final evaluation of the effect of supplementation, the relative progress of control and experimental partners in each of the fifty matched pairs was appraised. The results of this comparison are best observed in Fig. 3 in which charts for the 100 individuals are plotted. For convenience of interpretation, these have been arranged in decreasing order, based on superiority of gains of the experimental group. If only differences which exceed 0.3 log unit are considered significant it is found that such differences were observed in only twenty-six pairs (Fig. 3, 1-*A* and 3-*B*), and in twenty of these it was in favor of the subject which received the supplement. When the charts of individual subjects are examined it is noted that in the experimental group the final readings of only 11 are significantly better (in Fig. 3, those marked *), and those of nine are significantly poorer than at the beginning (those marked +). In the control group the final readings of six are significantly better and those of thirteen definitely poorer than on the first test.

That the vitamin A supplement given was probably large enough to produce maximum results is indicated by the fact that the fourteen experimental subjects who received the massive doses during the last two weeks responded no better than the others, with the possible exception of three cases whose readings decreased somewhat more than the general average.

COMMENT

In summing up the results of the different approaches made to determine the validity of the adaptometer test as an index of nutritional status with respect to vitamin A, it is apparent that little positive evidence for such a relationship was obtained.

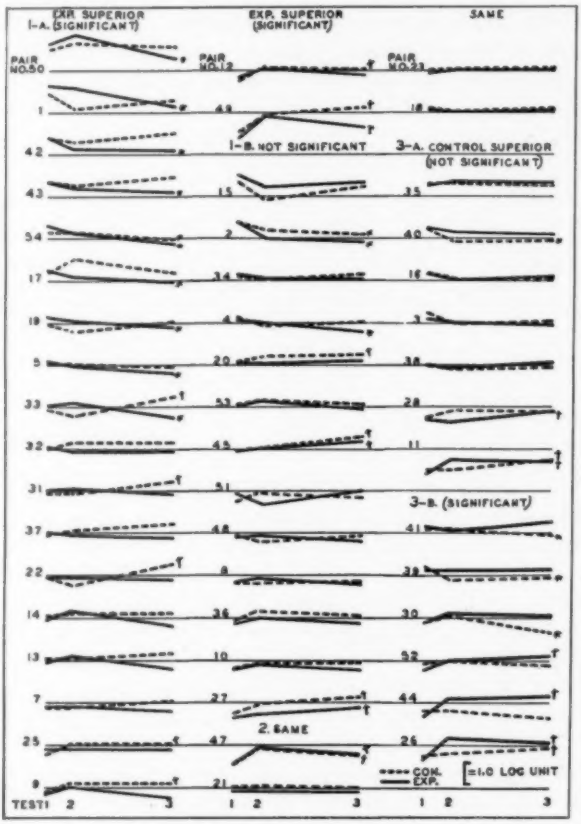

Fig. 3.—Dark adaptation of partners of matched pairs in each of successive tests.

The mean rod thresholds of the three groups of children from low, medium, and high socio-economic status, and whose dietary levels of vitamin A varied similarly, were almost identical. There was no correlation between adaptometer readings of individual subjects and their vitamin A intakes although the latter covered a wide range. Supplementation of the diets of fifty subjects with large amounts of vitamin A for a period of nine weeks, moreover, did not produce any striking results when their records were compared with those of the controls. Nevertheless, when the data are examined by all the meth-

ods of analysis, it is apparent that such differences as do exist between the progress of control and experimental subjects toward improved dark adaptation are almost uniformly in favor of the one which received the supplement. These differences are most pronounced in the few subjects who started with the highest rod plateau readings. These findings are almost identical with those obtained in the former study when the biophotometer was used for evaluating the dark adaptation of similar groups of children.

In terms of the validity and practical usefulness of the test, these results can obviously have only two interpretations: (1) that practically all the subjects were already receiving adequate amounts (or had sufficient stores) of vitamin A for normal dark adaptation, or (2) that the test does not sharply identify mild cases of vitamin A deficiency. The first explanation is an entirely possible one. If it is accepted, however, it must also be concluded (1) that vitamin A deficiency is probably relatively uncommon in the city of Chicago, and (2) that the vitamin A requirement is much lower than has been commonly proposed. Both these assumptions are plausible. The subjects in Group A came from one of the poorest sections of the city and had the general appearance of being very poorly nourished. The best record of vitamin A intakes that could be obtained indicated that 41 per cent were having less than 40 international units per kilogram per day and 11 per cent less than 20 international units. Yet only fourteen out of 100 children had subnormal dark adaptation as measured by the test, a proportion almost identical with that of the children in the two groups of more favored socio-economic status whose intakes appeared to be much higher.

Neither the minimal nor the optimal vitamin A requirement of children has as yet been established. Estimations of requirements have, however, varied widely. For a 10-year-old child weighing approximately 32 kg., the allowances suggested have ranged from 640 to 8,000 international units or from 20 to 250 international units per kilogram. It is quite possible that the lower figure may eventually be established as nearer to the minimum requirement. If so, it is reasonable to conclude that vitamin A deficiency does not exist to any great extent in the Chicago area, even in sections where general malnutrition may be quite prevalent. This theory is not difficult to accept, for vitamin A is fairly ubiquitous; it is supplied in amounts up to 10,000 to 25,000 international units per serving in greens and some of the other common foods, and since excesses may be stored in the liver, even an occasional serving of such foods might keep the minimum needs for the vitamin supplied. Before this conclusion is finally accepted, however, the possibility of other interpretations of the data should be considered.

As already indicated, the results of this study, as well as those of Lewis and Haig,[8] might also mean that the test does not differentiate between levels of vitamin A status in normal and borderline areas. This

is in no way inconsistent with the findings of Hecht,[3, 4] Booher,[6] Wald[5] and their co-workers, that subjects kept on depletion diets do eventually show markedly impaired dark adaptation. It may merely mean that no subjects in this study were on levels of vitamin A low enough to deplete their stores, with the exception of the fourteen subjects with high original readings, of whom the seven experimental subjects improved their status under vitamin A supplementation.

These results are what might be expected if it is assumed that the limits of the normal zone suggested by Hecht are also applicable to children as the present study indicates to be the case. The variation in dark adaptation of the subjects studied would thus represent only the normal variability commonly found for all physical measurements (again with the exception of those who had rod plateau readings above 3.5 log units). It would not be expected, therefore, that within this normal area differences in vitamin A intake would be related to adaptometer readings. This is in accord with the findings of Hecht and Mandelbaum[4] who state "that within the normal range the rod threshold level itself cannot be taken as an index of the nutritional state of an individual."

The facts that subjects receiving the supplement did improve slightly more than the controls and that this difference was more manifest in the subjects with the highest original readings, do, it is true, lend some support to the validity of the test. This is a long way, however, from indicating that the test is useful in practical situations in assessing the nutritional status for vitamin A. To serve such a purpose, it should be possible to apply the test to a school population or community, range the rod readings in a series from lowest to highest, and rate the nutritional status for vitamin A accordingly. A glance at Fig. 1 is sufficient to show that any attempt to make such a classification for the children of the present study would have led to gravely erroneous conclusions. It is probable, as indicated by the work of Hecht and others, that all markedly depleted subjects will show impaired dark adaptation. The present study would seem to indicate that few Chicago children would be found to be in this condition. It must be concluded in any case that the test has no great usefulness in classifying children for vitamin A status within the range of intakes and adaptometer readings represented in the Chicago area.

There are some indications that the retina of the eye may not after all be the first tissue to show the effects of a vitamin A deficiency. Popper[11] found the vitamin still present in the retina of experimental animals after the stores in the liver had been completely depleted. This finding has been confirmed in our laboratory.[12] Steffens, Bair, and Sheard[13] found that abnormal skin conditions occurred in subjects on an A-deficient diet before changes in retinal sensitivity and suggest this as a possible approach. Lehman and Rapaport[14] have also reported the occurrence of abnormal skin conditions which improved with vita-

min A therapy. However, subnormal dark adaptation was also present in their subjects. Hecht and Mandelbaum,[4] on the contrary, found no skin changes in their subjects all of whom developed impaired dark adaptation. On the other hand, two groups of workers (Yarbrough and Dann,[15] Lewis and co-workers[16]) have reported that their results indicated the level of vitamin A in the blood to be the most promising single method of determining a deficiency. These findings suggest the desirability of exploring other possible approaches to the problem, as well as further studies with the adaptometer on subjects having even lower intakes of vitamin A than those represented by the poorest group in the present study.

SUMMARY

The purpose of this investigation was to determine the reliability of the adaptometer test and its validity as a measure of the nutritional status of children with respect to vitamin A.

Three groups of children from different socio-economic levels were tested and accompanying dietary studies were made on two of the groups to determine the amount of vitamin A in their diets. It was found that:

1. The mean rod thresholds of the three groups of children known to have had widely different vitamin A intakes were almost identical.

2. Approximately the same per cent of the subjects in each group had subnormal dark adaptation.

3. There was no correlation between adaptometer readings and daily vitamin A intakes although a number of children were apparently receiving less than 20 international units per kilogram per day in their diets.

Fifty matched pairs of children were selected from the group whose subjects were found to have the lowest vitamin A intake. One of each pair was given 25,000 international units of vitamin A each school day for a period of nine weeks while the other served as a control. Both control and experimental subjects were retested after two weeks and again after nine weeks of supplementation. Analysis of the results showed that:

1. A slight but significant improvement was found in the mean rod plateaus of the experimental children when compared with those of their control partners.

2. The effect of supplementation was most pronounced in individuals whose original rod thresholds were in the subnormal zone.

3. Significant improvement in rod thresholds was found in only eleven experimental as against six control subjects.

4. A slightly larger number of children had vitamin A labile thresholds at the end of two weeks' supplementation than originally had thresholds in the subnormal zone, but, in general, the same children were classed as deficient by both methods.

The above findings indicate either that the adaptometer does not measure the first signs of a vitamin A deficiency or that such a deficiency is uncommon among children in this area.

The collaboration of Lillian Nash, Annette Young, and Sadie Brenner is gratefully acknowledged. Miss Nash made both the dietary study and the adaptometer tests on the subjects in Group B. Details of her study were reported in her master's thesis, "Dark Adaptation of Children as Determined by the Hecht Adaptometer," University of Chicago, 1940. Miss Young conducted the dietary study on the subjects in Group A and reported it in her master's thesis, "Vitamin A Intakes Versus Readings on the Adaptometer," University of Chicago, 1940. Miss Brenner assisted in the standardization of the test procedure.

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A NEARLY FATAL REACTION TO SULFADIAZINE IN A TEN-YEAR-OLD GIRL, INVOLVING SKIN, EYES, AND OROPHARYNX

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J. G., a 10-year-old female was admitted to the hospital Jan. 11, 1942, critically ill, with a generalized pemphigus-like rash, high fever, and severe toxemia. Fifteen days before admission, the family physician had started her on sulfadiazine, 7.7 gr. every four hours for an acute follicular tonsillitis with acute bilateral cervical adenitis and high fever. The patient responded satisfactorily to this therapy, and in a few days there was subsidence of the nodes and fever. This dose of the drug was continued for eight consecutive days until Jan. 3, 1942, a total of fifty 7.7-gr. tablets having been given. On this date the mother took the patient to the physician's office, stating that the child was fine, the appetite was good, the cervical swelling had subsided, and the temperature had been normal for four or five days. The mother was then given a prescription for more of the drug and instructed to continue with 1 tablet three times a day. For some reason, she did not start the drug again until four days later, January 7. On January 9, two days later, a rash was noted on the child's face, the conjunctiva was somewhat injected, and the drug was stopped. The next day, January 10, the rash spread from the face to the chest, and the child developed a temperature of 103° F. The following day, January 11, the rash became generalized, she complained of a very sore mouth, the fever increased, and the physician sent her to the hospital.

On admission physical examination revealed the patient to be critically ill, somewhat drowsy, and very toxic. The skin showed a generalized erythematous maculopapular rash which was confluent in large areas. Almost the entire skin of the body was involved, there being just a few scattered areas of normal skin. There were enormous numbers of vesicles and large bullae present, varying in size from 2 to 3 mm. in diameter to the size of a silver dollar. In some areas, the superficial layer of skin was loosened and could be pulled away easily. The ocular and palpebral conjunctivae were markedly injected. The eyelids were swollen shut. The mucous membrane of the oropharynx, including cheeks, tongue, and pharynx, was covered completely with a thick white membrane and broken bullae. The temperature was 104° F.; pulse, 144, respirations, 40. The examination of the ears, chest, abdomen, and nervous system was essentially negative. Our clinical impression at this time was a pemphigus-like rash due to sensitivity to sulfadiazine or some severe overwhelming infection. The patient was seen on the same day by our consulting dermatologist, Dr. J. J. Eller of New York, who agreed that most likely the case was one of a drug reaction, provided acute infectious mononucleosis and an overwhelming infection were ruled out by blood studies.

The blood count on admission showed hemoglobin, 84 per cent; red cells, 4.6 millions, white cells, 8,000 with 86 per cent polymorphonuclear neutrophiles, 13 per cent lymphocytes, and 1 per cent monocytes. The patient's condition was critical during the first week, the temperature ranging from 101° to 104° F. and the pulse averaging about 140. She was unable to take anything by mouth for several days and daily large amounts were given of 5 per cent glucose with Hartmann's solution, plasma, ascorbic acid, and thiamine chloride, by vein during the first

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week, after which time she was able to take sufficient fluids and nourishment by mouth. During this first week, the eyes developed a very severe pseudomembranous conjunctivitis. There was considerable exfoliation of the corneal epithelium and edema of the iris, especially of the right eye. On the seventh hospital day, the blood count was: hemoglobin, 73 per cent; red cells, 4 million; white cells, 9,500 with 22 per cent segmented and 13 per cent non-segmented polymorphonuclear neutrophiles, 37 per cent lymphocytes, 23 per cent eosinophiles, and 5 per cent monocytes. The urine on admission showed a trace of albumin. During the first week on two occasions there was a heavy trace of albumin. Later urinalyses were negative. The blood culture and culture from a bleb taken on admission were both sterile. The heterophile sheep red cell agglutination test was negative. Sulfadiazine determination of blood on admission was less than 1 mg. per cent per 100 c.c. of blood. The urea N determination was 23 mg. per cent on the fifth day.

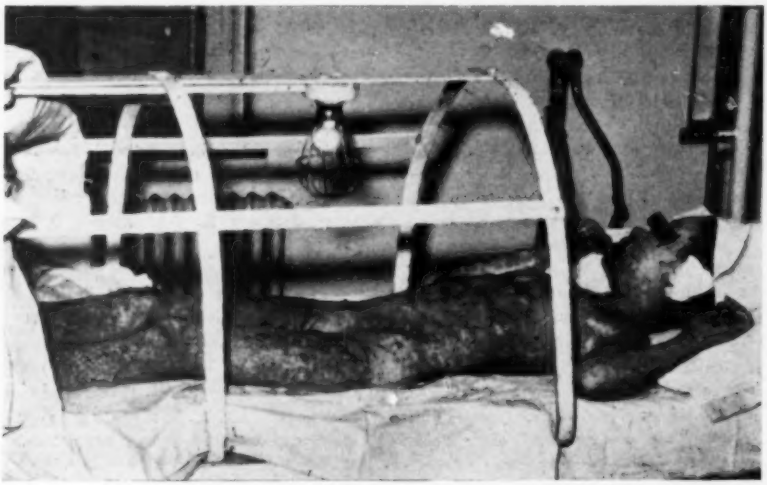

Fig. 1.—Condition of the skin fifth day after admission.

During the second week the temperature subsided by lysis from a level of 103° to about 100° F., and the child's general condition was improved. The pulse decreased from about 130 to 90 per minute. The condition of the skin was showing improvement, with areas of new skin appearing underneath the drying bullous areas. The condition of the mouth improved gradually with sloughing off of some of some of the membranous lesions. At this time almost a complete membranous mold of both lower and upper conjunctival fornices of right eye was removed. There was still considerable conjunctivitis, swelling of lids, and photophobia present.

During the third week, she continued to improve and the temperature ranged between 99° and 100° F. The skin showed gradual improvement with considerable desquamation and a return to a more normal appearance. Many fading, moderately pigmented patches indicated where previous bullous lesions had been present. The mouth was improving and she was taking soft foods well, although the lips were still swollen. Despite careful observation, both eyes showed several small and large webs due to a symblepharon formation. The webs were cut and good functional result was obtained. She continued to have some conjunctivitis and photophobia for several weeks. She remained in the hospital for three additional weeks,

six weeks in all. When discharged the child was in good condition and completely recovered except for some residual conjunctivitis, for which she was referred to the care of an ophthalmologist.

Fig. 2.—Appearance of the skin seventeenth day after admission. The tongue was red and edematous following desquamation.

From the history and progress of this case, it seems reasonably certain that the clinical picture represented a reaction to sulfadiazine. The drug was administered in full doses for eight days, followed by a period of four days in which none was given. It was then given again in small dosage for two days. Perhaps this circumstance provided a basis for the development of a hypersensitivity to the drug with subsequent reaction occurring on its resumption. Conjunctivitis is sometimes seen as a reaction to sulfadiazine. The eosinophiles of over 20 per cent on two occasions would fit in with an allergic reaction. The case is presented to show that under some circumstances, sulfadiazine, up to now regarded as less toxic than the previously accepted drugs in the sulfonamide group, can produce serious and possibly fatal reactions.

HYPOPLASTIC CONGENITAL ANEMIA

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DURING the past few years several reports appeared in the literature of a peculiar form of anemia in infancy. All the cases described had certain features in common and did not fit into any of the accepted classifications. They were characterized by a hypoplasia rather than an actual aplasia of the bone marrow elements. Erythropoiesis only was affected, while the leucocytes and platelets were normal or only moderately diminished in number. There was no hemorrhagic tendency. None of the generally used dietetic or medicinal measures had produced the slightest improvement and the patients could be kept alive only by repeated transfusions.

Blackfan and Diamond,[1] in 1938, reported four such cases and mentioned four others that they had heard about. In the discussion of this report, Hugh Josephs cited two cases he had had under his care. In all these cases the erythrocytic elements were involved, while the leucocytes and platelets were only moderately reduced. There was no evidence of blood destruction and no signs of regeneration. The patients were kept alive by transfusions, and both of Josephs' patients died when transfusions were discontinued.

Rinvik[2] has recently reported two similar cases. Both patients progressed relatively well with repeated transfusions.

Since September, 1938, I have had a patient under my care who, I believe, presents a very severe form of this type of anemia. In addition to a very marked reduction of the erythropoietic elements, the segmented leucocytes were almost nonexistent and the thrombocytes much reduced. It was only the progress of the case that enabled us to differentiate it from a true aplastic anemia.

H. S. was born June 28, 1938. The father's and mother's ages were 32 and 30 years, respectively. The family history revealed nothing of importance. An older child, aged 10 years, was entirely normal. Pregnancy and labor were uneventful. The baby's birth weight was 8 pounds, 1 ounce. At the age of 3 months the child was brought to my office for a routine examination and feeding instructions. There were no complaints except that the mother thought that the baby's color was not good. The infant had taken his feeding well and was gaining in length and in weight.

In examining the infant one was struck by the white, almost ghastly appearance of the skin and mucous membranes. The infant was otherwise well developed and nourished and was markedly active. His weight was 11 pounds, 12 ounces, and his length, 24 inches. The heart was normal, the liver and spleen were not palpable, and there was no adenopathy and no jaundice. The blood revealed the following: hemoglobin, 2.5 Gm. (17 per cent); erythrocytes, 750,000; leucocytes,

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2,500 with 8 per cent segmented cells; reticulocytes, 0.25 per cent; platelets, 180,000. There were no immature cells. There was marked poikilocytosis and anisocytosis. The icterus index was 5, and the van den Bergh test showed a negative direct reaction. The fragility test showed a beginning hemolysis at 0.40 per cent and complete at 0.28 per cent.

A transfusion of 150 c.c. of blood was given. This brought the count up to 44 per cent hemoglobin, two million red blood cells and 3,600 white blood cells. The child's color improved, the appetite continued good, and there was progressive gain in weight and in length. However, within ten days the pallor returned, the blood reverted to the original picture, and another transfusion was given. In all, thirteen transfusions were given at intervals of from two to six weeks.

Roentgenograms of the long bones taken at 4 months of age revealed regular bands of increased density on the metaphyseal border of the epiphyseal line, indicating periods of cessation of growth. At 7 months of age an x-ray of the right tibia revealed a dilatation of the medullary canal caused by bone atrophy.

A sternal biopsy was performed when the child was 11 months old and was reported by Dr. I. Davidsohn, pathologist, as follows: The predominant cells are immature nucleated red blood cells. They vary from megaloblasts, which are occationally present, through macroblasts and normoblasts. The myeloid cells are present, but the myeloblasts are rather scarce. Megakaryocytes are fairly well represented. The impression is that of a vividly regenerating red bone marrow and of a less marked regeneration of myeloid cells. There is no evidence of anything that would suggest a leucemia. The deviation from the normal is more quantitative than qualitative.

The maximum count obtained after a transfusion was two million erythrocytes and 44 per cent hemoglobin, but this seemed entirely adequate for the patient, whose color was good and whose growth and development were normal. It was not until the count dropped to one million and the hemoglobin to 20 per cent that the extreme pallor returned. These levels were used by us as indications for transfusion.

On March 13, 1940, at the age of 21 months, 200 c.c. of blood were infused. On the following day the blood revealed 10.7 Gm. (64.2 per cent) hemoglobin, 2,800,000 erythrocytes, 3,500 leucocytes with 27 per cent segmented cells, 0.9 reticulocytes, and 182,000 platelets. This picture was maintained for several months, except that on one occasion the platelet count dropped to 40,000. From then on the blood picture showed progressive improvement with no further transfusions. A study of the blood at 3 years of age revealed the following: 12.4 Gm. (72 per cent) hemoglobin, 3,580,000 erythrocytes, 10,000 leucocytes with 60 per cent polymorphonuclear neutrophiles, 35 per cent lymphocytes, 3 per cent monocytes, 0 per cent eosinophiles, 1 per cent basophiles, and 1 per cent plasma cells. No basophilia of the granules of the neutrophiles; denseness of the erythrocytes was normal; reticulocytes, 9.1 per cent; platelets, 64,000 per cubic millimeter. Erythrocytes size less than 7.5 microns, 4 per cent; 7.5 microns, 24 per cent; larger 74 per cent. This count was made by Dr. Raphael Isaacs.

Thus at 3 years of age the blood still reveals a moderate anemia of a normochromic macrocytic type. The general development at this time seems somewhat below the average as to height and weight, and the child seems somewhat listless.

The outstanding feature in this case was an apparent inability of the bone marrow to produce blood elements, involving not only the erythrocytes and hemoglobin, but also the granulocytes, and to a lesser extent, the thrombocytes. This deficiency of the bone marrow was apparently temporary in nature, as spontaneous blood generation began at 21 months of age.

An interesting feature of this condition was the remarkable recuperative power of this infant and his resistance to infection. During epidemics of upper respiratory infection he was often the only member of the family to escape the common cold, and, if infected, would be the first to get well. At 7 months of age he suddenly developed a temperature of 105° F., became very toxic, and revealed typical physical and roentgenologic findings of bronchopneumonia. The blood count at the time revealed 1,200,000 red cells, 3.9 Gm. of hemoglobin, 3,700 white blood cells, of which 32 per cent were polymorphonuclears. It seemed obvious that this was a terminal affair and the family was so notified. To the amazement of all concerned, improvement began on the fourth day, the temperature dropped by lysis, and complete recovery occurred within one week.

The etiology of this type of anemia is unknown. The possibility of a metabolic disturbance involving some blood-building substance is suggested by Blackfan and Diamond. The prognosis, as judged by our case, is apparently good if transfusions are given frequently enough to tide the child over the period of bone marrow inactivity. The difficulties of giving repeated transfusions to small infants are obvious, and intramedullary infusions may have to be resorted to.

SUMMARY

A case of congenital hypoplastic anemia is presented. The outstanding features were a severe diminution in the erythropoietic and granulocytic bone marrow elements with a less marked decrease in thrombocytes. There were no evidences of blood regeneration or of destruction. Life was maintained only by repeated transfusions, and none of the blood-producing substances were of any value. The infant seemed able to adjust himself perfectly to low hemoglobin and red cell levels. In spite of rather low platelet counts there was no hemorrhagic tendency. At the age of 21 months the count suddenly began to rise and at this writing is practically normal. No etiologic factor was discovered. An interesting sidelight is the remarkable resistance to infection and recuperative power of this infant, even during periods of profound anemia.

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QUANTITATIVE COLLECTION OF URINE FROM INFANTS AND YOUNG CHILDREN

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IN MANY clinical and research studies on infants, complete twenty-four-hour urine specimens, uncontaminated by small amounts of fecal matter, are required. This necessitates having a urine collector which is not only reliable, but also offers a minimum amount of discomfort and is serviceable for more than twenty-four hours after application.

Means for the quantitative collection of excreta from infants and small children have been reported.[1-6] Several of the earlier methods[2-4] are involved and require special equipment not available in the average hospital. This paper presents the description and procedure for making a urine collector which has proved to be highly efficient, inexpensive, and comfortable to the young subject.

The harness described is a modification of the one* used by Dr. Elizabeth Knott, Department of Pediatrics, University of Chicago Clinics. This means for quantitatively collecting urines from infants has been completely satisfactory in our experience with male infants.

METHOD

Equipment.—

1. Cloth (percale or muslin) 6 inches square.
2. Soft lead pencil.
3. Adhesive plaster.†
4. Penrose drain.‡
5. Fine dissecting scissors, 25 mm. blade.
6. Collecting bottle.
7. Rubber tubing to connect penrose tubing with collecting bottle.
8. Metabolism bed.
9. Restraints.
10. Cotton batting.

Procedure.—

The harness is made from a rectangular piece of adhesive plaster. The length and width are determined by the anatomical measurements of the individual from whom urine is to be collected. The measurements

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*An adaptation of the urine collector originally devised by Dr. Genevieve Stearns, Department of Pediatrics, University Hospitals, State University of Iowa, Iowa City, Iowa.

†Made by Johnson & Johnson in five-yard rolls that are 12 inches wide.

‡Sold in diameters ranging from ¼ to 1 inch and in 36-inch lengths, V. Mueller & Co., Chicago, Ill.

are obtained by placing the infant in a supine position; the thigh and the legs are flexed and the legs are abducted and externally rotated so that the infant is in a position resembling that of lithotomy. While the infant's legs are held in this position, a piece of soft material (e.g., percale or muslin) is placed over the area of the genitals and pushed back under the scrotum. The length is measured on the cloth by marking off the lower abdominal region (just above the symphysis pubis) and the gluteal fold. At this time the cloth is marked at the site of the proximal end of the anterior surface of the penis and at the perineal surface just anterior to the anus. The width of the rectangular piece of adhesive is determined by penciling off the side-to-side extent of the widest portions of the pubic region. Continuation of both of these lines of demarcation down the median aspect of the upper part of each thigh will give the correct degree of tapering to the section covering the scrotum (see Fig. 1).

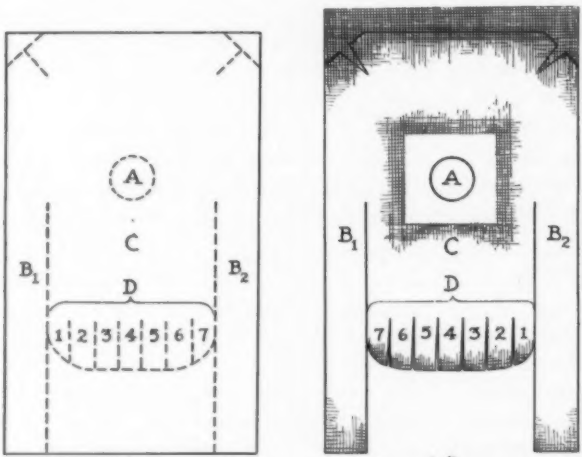

Fig. 1.—*A*, Site of attachment of penrose drain; B_1 and B_2, strips that are extended down the median aspect of the upper part of the thigh down to the gluteal folds; *C*, section covering the scrotum; D_1 to D_7, tabs cut at the bottom of *C* to be tucked underneath the scrotum and attached at the perineum.

The next step is to find the narrowest penrose drain which can be easily pushed over the penis. The diameter of the selected piece of penrose drain (in rounded position) gauges the diameter of the opening for the penis (Fig. 1, circle *A*). The length of the penrose drain is measured by approximating the best point to attach the rubber tubing leading into the collection bottle.

The piece of rectangular adhesive plaster is cut according to the broken lines in the pattern presented in Fig. 1, *1*. Care must be taken that the diameter of circle *A* will permit perfect fastening of the penrose tubing. (The opening must not be too wide nor too narrow.) The crinoline backing (indicated by the cross-hatched areas) is separated from the adhesive plaster and is cut off about ⅜ to ½ inch below circle *A*. The cut piece of crinoline is reattached at a level of ⅜ to ½ inch above circle *A*. This leaves an exposed adhesive area only around the opening for the penis. The adhesive side of the harness should now appear as in Fig. 1, *2*.

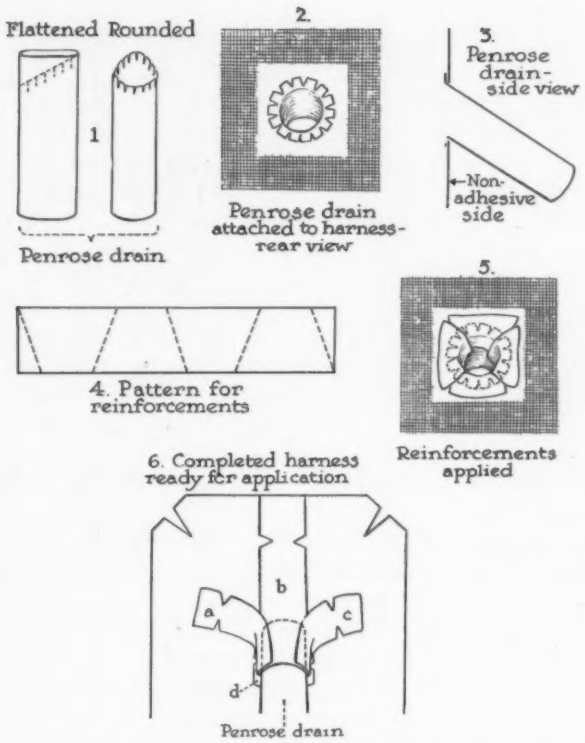

Fig. 2.

The top of the penrose drain is flattened between the index and middle fingers. It is cut on a bias and fringed according to the representation of the flattened form in Fig. 2, *1*. Each latex tab is approximately 3 mm. wide and 2 to 3 mm. deep. When ready for attachment to circle *A* it should appear as the rounded form shown in Fig. 2, *1*.

The drain is introduced into circle *A* by placing it underneath the nonadhesive side of the harness and pushing up about ½ inch of the

tubing through circle *A*. The peak of the drain is attached at the top of the circle. Each tab is fastened to the adhesive plaster as shown in Fig. 2, *2*. This procedure spreads each tab apart so that a notch is formed between each section. Each notch should be formed 2 to 3 mm. outside of the perimeter of circle *A*. The walls of the penrose drain should fit smoothly into circle *A*. When fastening of the latex tubing has been completed, the tube is gently pulled to test for the possible formation of any leaks around the periphery of circle *A*.

Viewing the penrose tubing from the nonadhesive surface of the harness, it should slope downward as in Fig. 2, *3*. The penrose drain is reinforced by four pieces of adhesive plaster cut in the shape of isosceles trapezoids. The reinforcements are cut from a strip of bias adhesive plaster about 20 mm. wide (see Fig. 2, *4*). The reinforcements are placed first at the top and bottom of the latex drain and then at the sides. All of the tabs and notches of the penrose tubing should be completely covered; the reinforcements should extend at least 4 mm. around and below (i.e., down into the tube) the perimeter of circle *A* (see Fig. 2, *5*). To insure perfect attachment of the tube to the harness, the reinforcements inside the walls of the tube are firmly pressed with the corresponding upper portion of the reinforcement covering the tabs of the penrose drain. To increase the adhesive area around the penis, the nonadhesive surface of a piece of adhesive plaster is fastened to the adhesive surface of the harness so that the reinforcements are completely covered. This piece of adhesive extends across the harness completely covering the width of section C (see Fig. 1) and ending at strips B_1 and B_2. It has an opening which perfectly coincides with circle *A*. Finally the middle portion of the adhesive side of the collecting device is covered with crinoline.

The penrose drain is reinforced (see Fig. 2, *6*) with four strips of adhesive tape (*a*, *b*, *c*, and *d*) on the front nonadhesive side of the urine collector. The top and bottom reinforcements (*b* and *d*) are applied first, and finally the side pieces (*a* and *c*) are attached. Notches are cut into each strip to make it fit smoothly around the walls of the tube and flat against the harness. The urine-collecting device is now ready for use.

Warming the harness on a hot metal lamp shade just before application increases the adhesive properties of the plaster. For the application of the collector the infant is held in a position resembling lithotomy. First, the middle piece of crinoline is removed. The infant's penis is inserted into the penrose drain and the adhesive plaster surrounding the penis is smoothed and firmly pressed into place. The adhesive plaster must always fit smoothly and tightly. Second, the upper piece of crinoline is removed and the adhesive plaster is fastened over the entire pubic region and adjacent lower abdominal region. Third, the bottom

piece of crinoline is removed and the plaster is extended downward to cover the scrotum completely. Adhesive plaster must always be between any two surfaces of skin. The tabs D_1 to D_7 (Fig. 1) provide a means of smoothly fitting the adhesive plaster underneath and around the side of the scrotum. The attachment of the tabs ends around the perineum. Finally the side strips B_1 and B_2 (Fig. 1) are fastened to the thighs along the median aspect and down to the gluteal folds. A strip of adhesive tape is placed underneath the scrotum to reinforce the tabs ending around the perineum. Rubber tubing leading into a collection bottle is attached to the outlet of the penrose drain.

Fig. 3.—Photograph of infant on metabolism frame with collecting harness in place.

The infant's legs are kept apart by restraints lined with cotton batting being placed around his thighs and ankles. The restraints around his thighs are pinned to the bed sheet and mattress (or canvas of the Bradford frame if stools are being collected), and those around his ankles are anchored to the sides of the bed by long strips of a strong material. This type of restraint enables the infant to move his legs without disturbing the collecting apparatus. An older infant requires a band of material placed across his chest and under his arms; it is fastened to the mattress or bedsides to keep him in position. The mattress or Bradford frame is slightly elevated at the top to facilitate drainage and to permit the child to sit up occasionally (only in the presence of an attending nurse) without shutting off the penrose drain.

Some subjects have worn a harness without the development of any leaks for as long as five days. Occasionally only a fresh strip of adhesive to reinforce the tabs ending around the perineum was required. Removal of the adhesive-collecting device is a painless procedure because of the absence of body hair in infants.

With a few adjustments the urine collector described was used successfully on one occasion to obtain successive twenty-four-hour specimens from one female infant. On another occasion the latex drain was used as a sleeve to hold a small test tube collecting urine from a premature male infant weighing 1,700 Gm. Since each voiding was very small (2 to 3 c.c.) and emitted in drops, it was necessary to keep the infant's penis in the test tube to avoid any loss of urine. When the test tube was about one-third full, it was removed by the latex tubing being rolled back and another one was inserted. In this way, successive, complete twenty-four-hour urine collections were made.

SUMMARY

The method for making and applying a highly efficient, durable, comfortable, and inexpensive urine collector for male infants is described.

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The Pediatrician and the War

MEETING OF REGION III OF THE AMERICAN ACADEMY OF PEDIATRICS, CLEVELAND, MAY 14 AND 15, 1942

Remarks of the President-Elect, Dr. Borden S. Veeder, at the Luncheon Meeting, May 17, 1942

The essential thing before us is to win the war, an undertaking that may require several years. Everything else must be subordinated. Failure to win would mean that everything we have created and lived for would be lost, including the welfare of the child which has been the group endeavor that has united us in the Academy. To win the war will call for many giving their lives, and for all the relatively unimportant readjustment of the way of life we have been living, and the giving up of many things we have become so accustomed to that we have unconsciously come to regard them as essentials. Suddenly we are brought face to face with a new formulation of values.

In the same way that our economic life and structure has had to undergo a complete readjustment, a thing that so many as yet fail to grasp, so must our entire professional life and structure be reorganized and readjusted. To win the war the first essential is a trained equipped military force. Shortly our Army will be larger than it was in 1918 when World War I ended. Our present army organization calls for about 6.7 doctors per 1,000 men. To this must be added the Navy needs. The doctor is the only army officer whose necessary technical training calls for a preparation of at least four to five years. His place cannot be refilled with graduates of intensive courses, and hence the deferment of medical students. The first duty of the medical profession in a war such as this, whose outcome will determine our survival, is to the military forces. Just as the vast majority of soldiers must be as young and physically fit and active as possible, so must the army doctor as far as possible belong to this category. The demand for physicians in the Army, however, is such that within the last month, although we have been at war only five months, the upper age limit for commissions in the medical corps has been raised from 45 to 55 years of age.

Pediatrics is a fairly young specialty and hence it follows that many in our group are young men and hence will and must go into military service. I have before me the army medical officer requirements for 1942 as of March. It calls for 24,000 by Jan. 1, 1943, of whom 17,000 are in specialty categories as surgery, orthopedic surgery, neuropsychiatry, etc. Among the twenty specialties in the list, pediatrics is not included, unless, as in England, they are included among the 2,140 internists. They do fit into the last group of 7,000 general practitioners, which I take to mean younger men for regimental work. I have before me a list of names of forty-eight Fellows in active service, and I am sure it is quite incomplete, as names are being added almost daily. This list will increase rapidly, and I know further of many younger pediatricians, our recent hospital resident group not yet Fellows, who are in service. Seven men who appeared before the Board of Pediatrics Tuesday and Wednesday were in uniform. All honor to them.

Some sixteen months ago, almost a year before Pearl Harbor, before either you or I or anyone else knew what was in store for us, an editorial was drafted, approved

by the Editorial Board, and published in the February, 1941, issue of the JOURNAL OF PEDIATRICS which stated that warfare today was a total warfare and that the pediatrician would probably be of more value in civilian life than in service. None could foresee at that time the extent to which this world madness would reach. Today the situation is different. I am sure, although I have not consulted with them, that the group who thought as I did then, would agree that our first essential duty is to win the war and that only an overwhelming military force can bring this about, and all else must be subordinated.

Nevertheless one part of that statement holds true and that is that it is total warfare and it is a civilian war as well as a war of armed forces. Civilian morale and health must be maintained if the production of essential war materials is to be continued. Further the morale of the man at the front, and morale is an army essential, is infinitely better if he knows that those he has left behind, particularly his children, have adequate medical care. For those doctors who for one reason or another remain at home, and our government well recognizes the necessity for adequate civilian medical care, there is plenty of work to be done in helping win the war. One of our most pressing needs is for adequate medical and health facilities for the communities of munition workers who have migrated in swarms as a result of the war. Many are living in not only inadequate but bad housing, and in many instances medical care is inadequate. I imagine many of you have had similar experiences to those we have had in St. Louis. I know of several locations in these newly developed areas where there is great need for a pediatrician and where a trained man could do a great service, not a charity one, as charity is not asked, but there is no one to go. The older men have established responsibilities and the younger men who would ordinarily be available, although the condition would not exist ordinarily, must necessarily go into the Army. I am at a loss to know how to meet this pressing demand for trained pediatricians for the families of workers who are producing the materials of war except through governmental agencies who control today the distribution of physicians. Certainly within the next few months those of us not in military service will all have to work a lot harder, and, further, many of our spoiled patients of the past who expect the physician to be at their beck and call at their convenience must meet us on an entirely different basis than they have been accustomed. Another war readjustment.

The routine work of our hospitals and teaching institutions is undergoing drastic changes, and curtailment of past activities and refinements will continue. Perhaps after all it may not be a bad thing to learn how to differentiate better between the essentials and nonessentials in diagnoses and therapy, desirable as the latter may be. Inadequately equipped hospitals at the front and at the base in France in 1917-1919 did not prevent the staff from doing splendid medical work in the face of handicaps which in civilian life today would seemingly make good medical work impossible to those who have not lived through these experiences. It is the character and spirit and ability of the man which in the final analysis counts most rather than the tools which I think at times our present generation have overemphasized.

The "tag" that was hung upon these remarks today by the program committee was "The Academy and the War." To my mind the Academy and the pediatricians are synonymous, as the Academy is but the united voice and assembly of its 1,500 individual members.

Quite frankly I have been greatly preplexed at times as to just what the Academy as an organization could do. It would be rather silly, for example, to hold institutes on "war pediatrics" although quite definitely a function of other organizations whose medical fields are directly related to military medicine. We have tried to co-

operate and fit in wherever we could be of help or service, or thought we could be of service. In the end it has always seemed largely to revert back to what we as individuals could do. Since pediatricians as pediatricians are not needed by the Army, there has been no request or need for us to designate or select or nominate qualified individuals. The only exception to this has been the effort of Dr. Stokes' committee to place men trained in communicable diseases where they are needed and will be of most value.

Many of our Fellows have been interested in the problem of evacuation of children from areas liable to attack. The matter of care of refugee children which the Academy entered as an organization matter in 1939 has become a more or less dead issue due to war developments. We have been cooperating in every possible way with our national, state, and local official agencies, although conditions are so variable that what has been done has been again rather the result of individual efforts than a specific Academy undertaking. The picture may change at any moment as it has done so frequently in the past, and I can assure you that the Academy is ready to meet any request that may arise and fit into any situation in which it can be of the slightest aid or help.

We will win this war. No one can foresee, however, the readjustment in the practice of medicine as we have known it that will follow in its wake, but that they will be drastic is beyond question. They will be no more drastic, however, than the changes that will occur, and many have already occurred in every other walk of life. We can only meet the future with courage and fortitude, and I am confident that if we as pediatricians always hold in mind that the answer to every professional question centers on whether or not it helps the welfare of the child, all will work out to a good end.

The Physician (Especially the Pediatrician) and the War in Relation to:
LEE FORREST HILL, M.D., *Chairman*

1. The Selective Service.....Dr. Robert A. Bier, Major, M.C. U.S.A.
   From the Office of Selective Service Headquarters, Washington, D.C.
2. The Office of Procurement and Assignment.....Dr. E. L. Henderson
   Chairman, 5th Corp Area, Committee on Procurement and Assignment,
   Louisville, Kentucky
3. The Office of Civilian Defense.....Dr. William S. Keller, Senior Surgeon
   Resident, U. S. Public Health Service, Medical Officer
   5th Region, Cleveland, Ohio

CHAIRMAN HILL.—Members and guests of Region III: It is a pleasant duty indeed which has been assigned me in introducing our speakers of the evening. No subject is of greater concern to anyone in America today than the war. As physicians first, and as pediatricians second, we are vitally concerned to learn how and in what way we can be of greatest service in the present emergency, whether it be on the military or the civilian front.

Our speakers this evening have intimate knowledge of the gigantic problems which have already developed or are developing in connection with medical needs. I am sure we shall learn much from their remarks.

Our first speaker is Major Robert A. Bier of the Medical Corps of the Army of the United States. Dr. Bier trained in Cincinnati under Dr. Graham Mitchell. He is a member of the Academy of Region I and practiced pediatrics in Washington for twelve years. He was a lieutenant in the infantry in the last war. He has been in his present position as an assistant in the Medical Division of the National Headquarters at Washington since October, 1940.

The Physician and the War in Relation to the Selective Service

Dr. Robert A. Bier

They say you are supposed to start a speech or a talk with some little pleasantry, but not being good at telling jokes, I might tell you one of the things that happened the other day in the office just before I left.

Of course you know in Selective Service work we are concerned with two principal things, physical standards and classification, and one of the men came up with the very latest physical standards and said a man could be accepted for service if he could see lightning, hear thunder, and chew milk. As for classification, there seemed to be a new classification. I hope none of you will take this personally, as one of our officers did. It is the four "B's"—bald, bifocal, bridges, and a bulge.

Seriously, I want to tell you how much I appreciate having been asked to address you. I have been getting around the country somewhat, but this is the first time I have been among those that I feel are my friends and fellow pediatricians. I came to tell you something of Selective Service and its relation to you personally.

In order to orient you with reference to the whole picture of Selective Service, I shall attempt to give you some of the history and the background of it. Of course, most of this is known to you, but it will serve to refresh your memory.

The National Defense Act of 1920 laid the foundation of Selective Service. In Section 5-B of that act, the Congress of the United States decreed that the duty of the War Department General Staff shall be to prepare plans in conjunction with the Naval Forces for the mobilization of the manhood of the nation. In 1926 the Joint Army and Navy Selective Service Committee was created to study the best ways and means of procuring manpower for the defense of the country. This committee's function was restricted to planning the emergency procurement of manpower for our armed forces with a maximum of efficiency, economy, and equity, and with a minimum disturbance to the social, economic, industrial, and agricultural life of the nation. The plans formulated by this committee are now contained in the Selective Service Regulation and are known as the American Selective Service System.

It has been learned by experience that it was necessary to procure men by this compulsion method rather than by volunteer methods. It was also a more equitable way of procuring manpower to fight our wars. In addition to the need for the men to fight the war, it was also necessary to have an adequate supply of manpower for the industries essential to support the war effort.

The Joint Army and Navy Selective Service Committee was composed of a group of Reserve and National Guard officers, and in 1936 this was under the leadership of Major Lewis B. Hershey, who is now Major-General and Director of Selective Service. This committee, over a period of years, formulated the plans which later became the Selective Training and Service Act of 1940. You can see that for a long time the Government and the Army and the Navy have been cognizant of our need for plans for just such an emergency that has come upon us.

The Selective Service System consists of the National Headquarters and forty-eight state headquarters, with four other headquarters, one in Hawaii, Alaska, Puerto Rico, and the District of Columbia, and each state is divided into Local Boards; there are 6,441 of these Local Boards, and there is at least one Local Board area in each county or in a metropolitan area where there are 30,000 persons.

It is here that a just selection is made by the members who constitute the Local Board, which consists of three to five citizens of the community selected for their ability, integrity, and patriotism. These board members serve without pay in a position that is one of the most important and difficult in Selective Service.

It is estimated that there are about 175,000 persons working in Selective Service, and of these there are 27,000 physicians and 8,000 dentists, and 90 per cent of these people do not receive any compensation. This is, indeed, a splendid example of the unselfishness and patriotism of a large group of Americans, who are both outstanding and substantial citizens of their community.

Now the function of the Selective Service System, as you know, has been decentralized to the states and Local Boards. This provides for the classification in actual selection of each registrant by members of the registrant's own community, who are, in many cases, his neighbors. I am going into some detail in this, because many of you are going to be selectees, and I want you to know all you can about the actual operation of this important function. As you can see, the selection of these registrants for service for their own fellow members of the community and neighbors provides for a fair and equitable selection and leaves the decision of a man's value to his family, community, and nation to those who are in a position to know him best. Selective Service is truly selective.

This selection is not only to decide who shall serve in the armed forces, but also to insure the adequate production of essential materials for the nation at war. Selective Service attempts by acceptance, rejection, or deferment to place any man, especially of military age, where he can best serve the needs of the nation.

In order that a registrant may have every advantage and privilege accorded to him under the law, and to protect the interest of the Government, there are several advisory agencies to which the registrant may apply for counsel or present an appeal. There is assigned to each Local Board a Government Appeal Agent, who is usually a lawyer, and it is his duty to see that the best interest of both the Government and the registrant is served. In addition to the Local Board, there is what is known as an Advisory Board for registrants. There are several in each State. This Advisory Board consists of three lawyers and three other reputable persons. The chairman should be, if possible, a judge of a county court or court of similar jurisdiction.

This board acts as a legal counsel to the registrant when he fills out his questionnaire or gives any other advice which may be needed. There is a reviewing authority, known as a Board of Appeals. There is one or more such boards in each state for each group of 70,000 registrants. This board normally consists of five members which should include separate representatives from labor and industry, a physician, and a lawyer, and where applicable, a representative from agriculture. This board acts upon appeals or upon a claim of improper classification made by the Government or the registrant himself.

Thus the registrant is given every possible protection and at the same time the interests of the Government are safeguarded.

On Sept. 16, 1940, President Roosevelt signed the Selective Training and Service Act of 1940. I wish to remind you that at the time it was signed, the whole theme of national activity was based upon preparedness and training for defense. The act provided for common defense by increasing and training the armed forces under a fair and just system. The plan provided for a year of training, at the end of which the men were to be discharged and held in the reserve for an additional period of ten years.

While the act specified that men from 21 to 36 years of age should be called for service, it soon became evident that it was more practical to defer men of 28 years and over for military duty. As stated before, we were thinking in terms of training for defense, with no urgent need at the moment. Therefore, men could be brought into training with minimum disturbance to the social, economic, industrial, and agricultural life of the nation, as already outlined in the act.

In other words, an attempt was made to maintain business as usual. Now I am stressing this part of the Selective Service plan to show how it affected the medical profession. With the expansion of the Army for a peacetime program, it was thought that those physicians in the regular Army, the National Guard, and the Reserve Corps of the Army could adequately meet the needs of the training program. Therefore, Selective Service made ample provision for deferring the physicians because of the civilian need for their services. For this reason physicians were either placed in Class 3-A by reason of dependency or classified as 2-A, as being necessary to the maintenance of health, safety, and interest of the nation.

Now in considering the need for medical care for military as well as civilian needs, it was necessary to institute long-term planning. This was obvious because of the long period of study and training necessary to produce a competent physician. The problem of how to maintain an adequate supply of physicians, not only now, but in five and ten years, became apparent. Selective Service secured the splendid cooperation of the Surgeons General of the Army and Navy, the American Medical Association, and the Committee on Preparedness of the Association of American Medical Colleges. In the latter group were Dr. Rappleye of Columbia University, Dr. Burwell of Harvard University, and Dr. Diehl of the University of Minnesota.

With this splendid cooperation, especially of these three deans, Selective Service was able to institute a very liberal program of selection and classification of medical students under the law to insure an adequate supply of physicians for the future. The wisdom and foresight of this planning becomes more apparent every day.

This was the situation toward the end of 1941. Then came Pearl Harbor! With the declaration of war, the tempo of national military activity increased. From the program of training for defense, our country moved into the high gear of a strenuous war effort. In order to meet the needs of war and the changed situation, it was necessary to increase the powers and scope of Selective Service. There was urgent need for manpower not only for the armed forces but for the industries essential to war production. Civilian needs became secondary to war necessities. The veil of conjecture and wishful thinking that we would not become involved was now lifted, and we stood face to face with the grim realization that we were at war with desperate nations who would stop at nothing to gain their ends. It is now evident that we are engaged in a struggle that threatens our very existence as a nation.

On Dec. 13 and Dec. 20, 1941, President Roosevelt signed additional legislation, and with the amendments, the Selective Service law then became known as the Selective Training and Service Act of 1940, as amended. Briefly, a few of the major changes in the law are as follows:

1. The age limit was increased from 36 to 45 years and provided for the recall into service of those registrants 28 years or over who had been released from service prior to this time.

2. It required every male citizen and every other male person residing in the United States between the ages of 18 and 65 to register.

3. It removed the territorial restrictions as to service of persons inducted into the armed forces. You will remember that when Selective Service was first written, it provided the men would not be used out of the Western Hemisphere.

4. It extended the period of training and service from one year to the duration of the war and until six months thereafter.

5. It made liable for training and service every male citizen and every other male residing in the United States between the ages of 20 and 45. This latter group included aliens, both declarant and nondeclarant.

As you can see, this was an indication that the country was aware of the grim realization that we were embarked on a long and bitter war.

This question now faces us: What is our responsibility as physicians? Before Pearl Harbor, every consideration was given to insure full and proper health and medical care for our citizens. Now it becomes evident, as in all of our national endeavor, that civilian medical needs must be subordinated to our military needs. The Army is in dire need of thousands of additional physicians to serve in their forces, and a somewhat smaller number is needed by the Navy.

The offices of the Surgeons General report that they are in need of 5,000 physicians immediately, plus an additional 14,000 by January, 1943. With the possibility of an Army of 6,000,000 men, at the present ratio of six and a half medical officers for each 1,000 men, we shall need 39,000 physicians for the Army alone. Since the total number of physicians in this country is only 180,000, you can readily understand the problem which confronts the nation and the medical profession. This need is for physicians who are physically qualified to serve and who are young enough to stand rigorous military life.

The Medical Division at National Headquarters of Selective Service has attempted to keep the Director advised as to the supply and demand of physicians for civilian needs. That there has been a nationwide shortage of physicians is known to us all. For that reason, before Pearl Harbor, National Headquarters recommended that physicians should be deferred as far as possible, commensurate with civilian requirements and Army needs. Now, with the urgent need for physicians in the armed forces, National Headquarters has been requested to consider a reclassification of all doctors registered with Selective Service, with a view to making an adequate number available for service. While this step has not been taken, it is a distinct possibility.

Since war has been declared, deferment for dependency has been considerably curtailed. In fact, dependency acquired after Sept. 16, 1940, and more especially since Dec. 8, 1941, will not be considered except under certain extenuating circumstances. The problem of dependency is now undergoing extensive study, especially as applied to physicians, because they will become commissioned officers.

The most recent regulations in Selective Service concerning deferment for dependency provide for the subdivision of Class 3. In Class 3A will be placed those registrants who were deferred by reason of dependency and because they were engaged in an activity essential to the war program or support of the war effort. In the case of physicians, the matter of deferment for dependency, except in rare instances, may not be considered. The reason for this is that a physician when taken into the service will, in practically all cases, be commissioned with the appropriate compensation for the grade. This should, in most instances, preclude any actual hardship of dependents. I say hardship because we are at the stage now where anything short of hardship will be the rule rather than the exception and, gentlemen, if we should lose this war, what we now consider necessities will be luxuries.

Many physicians have been classified in Class 2A as men necessary in civilian activities. With the urgent need for physicians in the armed forces, Selective Service is contemplating the reclassification of those younger physicians who were formerly placed in Class 2A. Selective Service will look to the Procurement and Assignment Service for advise as to your indispensability or availability in relation to your professional standing and the need of your services in the community and will classify you accordingly. Just how Procurement and Assignment Service will function in this respect will be told you shortly by Dr. Henderson.

As mentioned previously, the medical student and interne are considered for deferment because of their greater future value to the country as trained physicians. Under Selective Service they will be deferred for only one year of hospital

training after graduation. Except in rare instances, no physician who is physically and otherwise qualified for military service will be allowed to continue his hospital training for more than one year. Men who are now in their postgraduate work in pediatrics or other specialties should arrange their affairs so as to be available to the armed forces on the completion of their course, unless sooner terminated by Selective Service or on direct call from the Army or Navy. It would appear to be unwise for any young physician, especially the pediatrician, to attempt to start practice. He should at once apply for a commission in the Medical Corps of the Army of the United States or the Medical Corps of the Navy and stand ready to do his part.

You may ask, what is the practicing physician's present status under Selective Service? With the urgent need by the armed forces for physicians, it will be necessary to take as many physicians, especially between the ages of 22 to 36, as it is possible to obtain, regardless of their specialty. The armed forces want young, healthy physicians for duty with combat units. A basic education in medicine with the usual major and minor surgical experience obtained in hospital training and private practice is sufficient. Special professional, technical, and tactical training to prepare these physicians for service with troops or aboard ship will be given after their entrance into the Army or Navy. There are a few permanent stations where the attending physician is called upon to care for children of the post, but the needs in this respect are either filled or so small as to be discounted. For all practical purposes, there will be no pediatrics in the Army.

I have been asked by pediatricians if they could not be used in contagious disease control. Here again the opportunities and needs are so small as to be amply covered by a few score of medical officers. From reports coming into the Surgeon General's office concerning contagious diseases among the troops, the incidence is a small fraction of 1 per cent.

Many of the younger pediatricians in practice and postgraduate training have complained that if they go into the Army for several years, they will forget their special training. If a pediatrician forgets in a few years of Army medicine all the pediatrics he has learned to date, it does not speak well for his mental ability or interest in the specialty.

There is much of practical medicine to be learned and used in the Army which is an asset to any physician. I refer to sanitation, hygiene, nutrition, control of contagious diseases, minor surgery, and general medicine. An Army physician must be adaptable. He must adjust himself to whatever duty he is assigned. The experience I have had in the past eighteen months has been of tremendous value to me, yet I have had very little clinical medicine as part of my duties, and I hope I have not forgotten my pediatrics.

As members of the American Academy of Pediatrics, I do not believe we flatter ourselves when we consider that we are leaders of the profession in the care of children. In spite of the position we hold both in society and the profession, the armed forces and, if necessary, Selective Service will reach out to take those of us it needs. In the latest report on the fellowship list, out of a total of 1,352 male members, there were only forty-six recorded as being in the armed services.

I do not believe this indicates any lack of patriotism or appreciation of our responsibility. It is more suggestive perhaps of the uncertainty in the minds of many of our physicians in this country, especially pediatricians, as to what part they can play in the war. In the present national crisis, we must think of ourselves as physicians and not as specialists in any particular field. While it is true that many of you by reason of age and professional attainments may not be available for military service, there are enough of us younger men who should take our place in the armed services. As regards your responsibility to Selective Service, those of you who are 44 years of age and under are definitely liable for military service.

We are advised by the Surgeon General's office that physicians up to the age of 55 years of age are being considered for active duty. Men in this age group may be commissioned in a grade commensurate with their professional attainment and standing. These physicians are not likely to be called upon for field duty but will be assigned to duties in the zone of the interior, such as base hospitals and other medical installations, thereby releasing for field duty younger and more active men.

Perhaps I have not painted a rosy picture of your future in reference to Selective Service. It is not my purpose to hold Selective Service over your head as a "big stick" to force you into the armed service, but unless the need for physicians is met in other ways, Selective Service is left no other choice and hence is prepared to supply the Army with any type of manpower including physicians and other specialized groups. The needs are apparent, imminent, urgent, and must be met by whatever means at our disposal.

Many young physicians have expressed concern for their economic security in the future. Unless we all put everything we have into this conflict, our future security, personal and economic, will be in serious jeopardy.

This, gentlemen, is the message I bring to you with reference to the pediatrician, the war, and Selective Service. Let all of us do our duty as we find it, and live up to the highest traditions of Americans and physicians.

CHAIRMAN HILL.—Our next speaker is one of those individuals who does not have to be much concerned about what to do with his leisure time. In addition to being chairman of the Committee on Procurement and Assignment for the Fifth Corps Area, which includes the states of Ohio, Indiana, Kentucky, and West Virginia, a position which he has held since Dec. 18, he is also a member of the Board of Trustees of the American Medical Association, he is president of the State Medical Association of Kentucky, he is president-elect of the Southern Surgical Congress, he is a member of the Southern Medical Association, and he is also chairman of the Executive Committee of the Southern Medical Association. In between, he carries on an active surgical practice in his home town of Louisville, Ky. I mention these things about him in order that we may not get the idea, as pediatricians, that we are the only ones who get a lot of jobs wished upon us.

The Physician and the War in Relation to the Office of Procurement and Assignment Service

By Dr. E. L. Henderson

IT IS a privilege and honor to be with you this evening although I feel somewhat out of place in a meeting of pediatricians because my work is an altogether different line. However, it is very much of a pleasure to be with you and I shall endeavor to tell you something about the Procurement and Assignment Service. I hope you will bear in mind that what I tell you tonight may not be true next week. Due to the acuteness of the situation, things are changing very rapidly in Washington.

Procurement and Assignment Service is the offspring of the American Medical Association Preparedness Committee. In June, 1940, the Surgeon Generals of the Army, Navy, and Public Health Service came before the Board of Trustees of the American Medical Association and requested them to appoint a committee to make some preparations in case of an emergency. As a result, the House of Delegates of the American Medical Association passed a resolution to have a Preparedness Committee appointed. The Speaker of the House of Delegates appointed the committee which was composed of a chairman and a member representing each of the nine corps areas in the United States.

This committee immediately made plans to correlate the information about the medical profession in this country and sent out questionnaires to the 186,000 physicians of the United States. Replies were received from about 160,000 physicians, of whom a large number expressed their willingness to volunteer their services to the armed forces in case of an emergency.

At the annual meeting of the American Medical Association here in Cleveland last year, the medical professional realized that other steps should be taken to prepare the country for an emergency, and the House of Delegates went on record as recommending some form of procurement and assignment for physicians. As a result of that, on Oct. 30, 1941, the President of the United States set up the Committee of Procurement and Assignment and appointed the Directing Board on December 22. Members of the Directing Board are: Dr. Frank Lahey, President of the American Medical Association; Harvey B. Stone, M.D.; James E. Paullin, M.D.; Harold S. Diehl, M.D.; Willard Camalier, D.D.S., who is Past President of the American Dental Association and represents the dentists; and Sam F. Seeley, M.D., M.C., U. S. Army, as Executive Officer. In turn, the Directing Board appointed Corps Area Committees, which were made up of a chairman, three doctors, two dentists, one veterinarian, one man representing medical education, and one representing hospitals. In addition, a State Committee representing each state was appointed. The State Committee appointed County and District or Councilor Committees, the latter for the more sparsely populated rural districts.

Procurement and Assignment Service was set up under the Office of Emergency Management as a part of the Office of Defense Health and Welfare Service, under the supervision of the Hon. Paul V. McNutt and more recently transferred to the War Manpower Commission. Procurement and Assignment is the responsibility of the medical profession itself. Only one member of the Board is a military or paid member.

The functions of Procurement and Assignment Service are: (1) to receive from various governmental and other agencies requests for medical, dental, and veterinary personnel; (2) to fill and maintain lists of professional personnel available, showing detailed compilations of such personnel; (3) to utilize all suitable means to stimulate voluntary enrollment having due regard for the public health needs of the nation and governmental agencies; (4) to provide especially for the equitable distribution of physicians, dentists, and veterinarians, not only in military service, but also in all governmental, industrial, and civilian agencies requiring assistance of physicians, dentists, and veterinarians for the duration of the war.

Procurement and Assignment Service is an honest effort to correct some of the mistakes that were made during the last war by assigning professional men where they were not prepared to serve. It is an endeavor to avoid putting square pegs in round holes and it also checks qualifications of all doctors enrolled.

In the questionnaires sent out just recently by Procurement and Assignment Service, every doctor, dentist, and veterinarian in the country was asked to name the service in which he would prefer to serve, in the order of his preference, giving four choices of service, whether in the Army, Navy, Public Health, Veterans' Administration, or other Federal Agency, or industrial medicine, or to retain his present civilian status. If you have not already done so, I urge every one of you to complete these questionnaires and return them immediately to the National Roster of Scientific and Specialized Personnel so that information may be kept up to date. As you know, there are a great many changes taking place every day in the medical profession, with about six thousand changes per month in the American Medical Directory. We must keep information up to date in order to function efficiently.

The present need of the Army is for approximately 10,000 medical officers by July 1 and 6,000 more by Jan. 1, 1943. That is a big order from Procurement and Assignment, but we are going to fill it. These physicians will be drawn from men

under 45 years of age, but principally from men under 37. Congress has said that every man between the ages of 20 and 45 is available for military service. The only exceptions are ministers and theological students. Every physician within selective service age limits should be enrolled with Procurement and Assignment Service as it is the only protection a doctor has against being drafted and serving as a private. Physicians under 45 years of age are the men who will comprise the main bulk of the Medical Corps of the Army and Navy.

All medical students, if physically fit, can enroll in the Medical Administrative Reserve Corps of the Army or Navy and after graduation be transferred to the Medical Corps of the Army or Navy. Any student who has received a letter from a dean of a Class A medical school can be deferred by taking that letter to his Selective Service Board. In this way, students will be protected from the Selective Service System. This also holds true for dental and veterinary students and enables them to complete their education and training and at the same time it keeps the supply of physicians constant. In other words, the Army and Navy are doing something for these professions never done before for any profession. A doctor entering the armed forces applies for a commission and, if he is physically and professionally qualified, receives a commission, the lowest being that of first lieutenant. Selective Service has recently said that whether or not a doctor has dependents makes no difference as to his availability because his salary as a commissioned officer is sufficient to take care of whatever dependents he may have.

Procurement and Assignment is the only agency that is prepared to give full information on any applicant. This is through the punch card system and the confidential information obtained by the American Medical Association which is now in the National Roster of Physicians and available to the Procurement and Assignment Service. There is complete information regarding 186,000 physicians in the United States, with complete appraisal of their professional status and all other available information. Of these physicians, 59,000 are 55 years of age or over, leaving 127,000 under 55 years of age. Of the last mentioned, it is estimated at least one-half cannot meet the physical requirements of the Medical Corps of the Army and Navy. Of the remaining 60,000, a certain percentage are already engaged in the armed forces of the nation and in other essential activities, such as medical education, hospitals, public health services, industrial medicine, and private practice.

I want to tell you that the response to Procurement and Assignment Service has been remarkable. The spirit of the three professions has been more than could be hoped for and the immediate needs of the Army and Navy are in the process of being filled. The success of Procurement and Assignment Service demands the complete cooperation of the medical profession. Since this organization was created to aid the medical profession in meeting the needs of the Army, the Navy, and the civilian population, physicians should accept the responsibility and enroll immediately. If you have failed to receive a questionnaire, write immediately to the National Roster of Scientific and Specialized Personnel, 916 G. St., N. W., Washington, D. C., requesting a form. If any man is holding out anticipating a higher rank, he is wrong. The men who go in first will get promotion first.

There has been considerable misunderstanding about the Committees for Procurement and Assignment Service. The Local Committee is simply to determine whether a man is available or essential in his community. The proof of whether or not a man is indispensable or physically unfit for military service rests upon the individual within that age group. The list of men who are available is sent to the State Committee, which then turns it over to the State Recruiting Board. No committee has any power to say who is going or who shall not go, and if any man is dissatisfied with the Local Committee's decision, he can appeal to the State Chairman and then to the Corps Area Chairman. Procurement and Assignment

Service is a voluntary service, but, in order to get the needed medical personnel, we are having pressure put on, and it is going to be put on stronger and stronger; men within the selective service age, if they are available, will almost be compelled to enter the service.

The majority of those called first will be within the age groups up to 36 years of age. Those who do not have special qualifications will probably receive a lieutenant's commission; those with special qualifications, or specialists, may receive a higher rank. Men under 45 should get in now. Men above that age group should wait for a call when there is need for men in greater numbers or in special lines of work. Those men will be called and given a commission commensurate with their age, qualifications, etc. In line with the rapidly expanding needs of the Army, it has been found necessary to lower the physical standards and put these men in limited service; that is, in the "zone of the interior" or in hospitals.

Recently, due to the congestion in Washington and the mistakes made in filling out application forms, there have been established State Recruiting Boards for physicians. I am sure that all of you know of doctors who made application for a commission one, two, or three months ago and who have not heard anything about it. Some of these doctors have even gone so far as to close their offices, tell their clientele they are going into the Army, thinking they are going in within the very near future, and then be very much disappointed because they have not received their commissions, and they cannot understand why. If you could be around the Surgeon General's office, you would realize that it takes a long time to get an application through, even longer since the number of applications has increased. Adding to the delay are applications incompletely or incorrectly filled out. As a result of the congestion, and in order to expedite granting commissions, Recruiting Boards have recently been set up in each state. These Boards are named by the Surgeon General and the Adjutant General and consist of two officers —a medical and a line officer—and two clerks. They will procure the names of all available physicians from the State Chairman for physicians of the Procurement and Assignment Service in your state. The Board will set up in the various localities at stated times to contact the men on the lists. They will have the authority to make final decisions on the application forms, to procure and make final decisions on the physical findings, and to administer the oath of office immediately to those who qualify physically and professionally who are under the age of 45 and who are to be given the rank of lieutenant or captain. For those physicians under the age of 45 who might apparently be qualified for rank above captain, the Board has the authority to initiate the applications and physical examinations and to forward the papers, with their recommendations, to the Surgeon General for commission. With applicants between the ages of 45 and 55, the Board has the authority to initiate the applications and physical examinations and to forward to the Surgeon General the papers and their recommendations. The Surgeon General will make the final decisions and commission those for whom there are vacancies in this age group. In this connection may I say that the Surgeon General will not commission a physician unless he is certified as available by his State Chairman of physicans for Procurement and Assignment Service.

Those men who filed applications for a commission several months ago and who have not heard anything from them can go to this Recruiting Board, fill out a new set of papers, go to any Army Hospital or post for their final type physical examination, or, if they have had an examination within the past ninety days, get a true copy, and then get sworn in by this Board and go to active duty in two weeks. The other papers in Washington will be held up so that there will be no "crossed wires."

As pediatricians, you may want to know how your special qualifications will be used by the Army and the Navy. May I say, that first of all, pediatricians are doctors of medicine. They have a fundamental medical education and can serve

as doctors wherever they are placed. It may become necessary to utilize pediatricians in various branches of the armed forces. Gen. C. C. Hillman, Personnel Officer in the Surgeon General's office, states that the special knowledge pediatricians have of infectious diseases will be utilized by assigning them to the infectious disease sections of station and general hospitals. Where such assignments are not available, they will, most likely, be placed on general medical sections of such hospitals. There is also a possible need for pediatricians in emergency base hospitals for the care of evacuated casualties.

Capt. F. R. Hook, Personnel Officer in the office of the Surgeon General of the Navy, told me that the Navy needed 175 pediatricians. The Navy takes care of the families of all their officers and many of the enlisted men and needs all types of specialists. They try as much as possible to keep every specialist in his own line of work, but there undoubtedly will be times when it will not be practical to do this. Pediatricians will be assigned to dispensaries and naval hospitals that are doing family practice. With a constantly expanding Navy, the need for physicians in the Navy increases.

In closing, I should like to have you bear this in mind. The armed forces need doctors *urgently*. We have been given the opportunity, or rather the privilege not as yet granted to any other professional group, of our own setup of doctors to provide this needed medical personnel. If we were to fall down on the job of supplying the medical officers, Selective Service would, in all probability, take over the job, for they must have medical officers. If we fall down on this job and it becomes necessary for Selective Service to do it, the Government in some other way will continue to do the job, after the war is over, and we are most sure to have some form of socialized medicine. If we are to continue the practice of medicine as we have in the past, it is essential that we do this job and do it now.

The medical profession has always responded most heartily and willingly when it has been called upon to render service, and we will do the same in the present crisis. I urge your complete cooperation in making Procurement and Assignment Service a success. To do this, we must have the help of every individual doctor. We are counting on it. We are out for victory in this war.

CHAIRMAN HILL.—Our last speaker will be Lt. Col. William S. Keller, Senior Surgeon in the United States Public Health Service and Regional Medical Officer for the Fifth Corps, which comprises the states of Ohio, Indiana, West Virginia, and Kentucky.

Lt. Col. William Keller was for a number of years a physician in the city of Cincinnati. For twenty-five years he was President of the Cincinnati Social Hygiene Society, and for twenty-three years he was a member of the Coordinating Committee of the Cincinnati Public Health Federation. For five years he was Chairman of the Syphilis Control Committee of Cincinnati, and during that time over 65,000 men in industry were examined for syphilis. This piece of work has been a very important factor in reducing lost man-hours of work in industry.

The Physician and the War in Relation to the Office of Civilian Defense

Dr. William S. Keller

I am always very much embarrassed at the introduction that is given me with reference to various things with which I am supposed to be identified, but I can assure you that the introduction is much more profound than the material involved.

Most of you, I know, came here to hear Dr. Henderson and the Major, who were assigned to talk on Procurement and Assignment. It is always true. We of the Office of Civilian Defense come in on the tail end of programs. Physicians flock far and wide to hear about procurement and assignment because they are very much interested. I have been on several programs with Tom Hendricks, Execu-

tive Secretary of the Indiana State Medical Society, and inevitably Tom Hendricks says, "I know what you are here for. You came here to know: What shall I do? When shall I do it? And what is going to happen to me after I do it?"

I think that is uppermost in all physicians' minds. It is natural and it is gratifying. It is as it should be, on all physicians' minds. But I must remind you, gentlemen, that there is a job for those of us to do who are at home, and it is a big job, and it is probably bigger than you think.

The other day General Hershey, here in Cleveland, told a story about the old lady who was working in a defense factory in England, and the Germans came over and bombed that factory. The rescue squads were pulling out people, and as they pulled out this old lady, they said to her, "Mother, is your husband in there?"

She said, "No, the coward! He joined the army."

Now, I realize perfectly well that that is a wrong analogy at this time. But who knows? And what I want to imply by that story is to tell you there is a big job for all of us.

There is one thing I can say about the Office of Civilian Defense, and that is, that we have had very good publicity agents. One thing we have had in Civilian Defense is good publicity. But there is one thing that these publicity agents did not tell you about the Office of Civilian Defense, and that is, that it is a planning organization and not an operating organization, and they did not tell you also that the Medical Department of the Office of Civilian Defense has had clear sailing from its inception.

Dr. George Baehr, who was a well-known internist in New York City, gave up a lucrative practice to become the Chief Officer of the Medical Department of the Office of Civilian Defense for a salary of seven thousand dollars a year, and he took into account at that time the best medical talent in this country, Dr. Lahey, Dr. Fred Rankin, Dr. Morris Fishbein, Dr. Cutler, and many other eminent physicians throughout this country.

There is another thing I want to tell you about Civilian Defense before I get into it, that it is not purely a defense program. It is also an offense program, because some of the doctors who remain at home will be expected to be on the offensive, with reference to part of our program.

Now in our Emergency Medical Units, pediatricians play a very important part, because we have instructed all of our Chiefs of Emergency Medical Services that surgeons should not be used on those committees, neither surgeons nor surgical nurses, that the Emergency Medical Field Units should consist of neurologists, pediatricians, and internists. We do not want the surgical staff of any of our hospitals to be disturbed. We do not want them disturbed because of possible emergency needs.

So, please, gentlemen, as you return to your various localities, if you have not been placed, take the place of surgeons who should be released from their various hospitals for emergency medical and surgical services.

In addition to the emergency medical field units that have been established, there is also a very great need for those doctors who remain at home to work with industry.

I wonder if it has occurred to you that as youth leave for war purposes, the age limit for people employed in industry will be increased? That will bring added medical responsibilities to industry, to defense industries. The tempo of industry will be increased and speeded. Increased hours of labor and production and added hazards and responsibilities must be assumed. As women enter defense industries, that will bring another problem, new problems to them and added problems for their families.

I need not remind you also that the physicians who stay at home will be responsible, more than they have in the past, for the indigent poor and the public charges, and, referring again to things that Dr. Henderson has said, it will be upon

the success and manner of that operation that is largely going to depend on how our profession will be permitted to operate after this world conflict is over.

I want to remind you also that we have an entire world that is seething in despair and troubled. We have more physicians and better physicians in this country than in any other country in the world. We have more nurses and better nurses in this country than in any other country in the world. But you cannot, gentlemen, starve nations for periods of from two to four years, you cannot blow up sewers, you cannot blow up water mains, you cannot have all that is coincident as the result of this conflict, without having a world after this conflict is over badly in need of public health supervision.

Not only during the war, but in the postwar period physicians will have an added responsibility, those who stay at home. I mean you are going to do double duty. One thing that those who remain at home will have to learn from the very start is not to be too acquisitive. Those who remain at home must maintain the ethics of the practice of medicine, guarding the interests of those men who have gone into military service, and their interest and acquisitiveness must be taken into consideration. It is the interests of your brother, who has been willing to fight for your democracy and mine, for which you are responsible. It is that very important thing of medical ethics which we must take into account, so that when that man returns from military service he will not be as far in the rear as he thought he would be.

I say that great responsibility will be placed upon the men who remain at home as well as the men who go into military service, and on that group at home will depend the manner and kind of practice of medicine that we may continue in the postwar period.

How are you who remain at home going to solve the problem of the need for emergency medical beds? At the present time we have no emergency medical beds. Conditions have arisen as a result of the hospital care plans, hospital insurance, public health education and from manner in which people live today in efficiency apartments, whereby they cannot be housed properly and must be cared for in hospitals. Then too, 20 per cent of the patients in some hospitals are there for clinical diagnosis. Maternity patients also are universally being sent to hospitals, and other persons, because they have two weeks' hospital insurance, take advantage of it for rest cures. All of these, gentlemen, are creating for our Office of Civilian Defense a very great emergency. No emergency beds.

Yes, you will be put to more inconvenience than that when luxury nursing disappears, and it is going to disappear, because we are not getting enough nurses for our armed forces. When eight-hour duty disappears our nurses will return to group nursing, one nurse taking care of maybe three or four patients, instead of eight-hour duty, three nurses in twenty-four hours.

Office nurses are no longer a logical claim, gentlemen, on the nursing profession today, and that will hit some of the pediatricians pretty hard. Nurses are going to have to be done away with in offices if we get anything like the number of nurses that we are claiming for the Army and Navy today. The Army has 8,000 nurses. They are asking for 10,000 more. One thousand nurses a month are requested. If the enemy sets foot on American soil, they will ask for 50,000 more.

We are faced with a very strange paradox, gentlemen, plenty of nurses on the nursing registry, but few nurses wanting to nurse in hospitals, and comparatively few nurses who want to join up with military forces. More are coming in recently. And that is another problem we will have to face. When the hospital care plan came into effect and money was accrued as a result of that plan and hospitals paid off their indebtedness and put in new terrazzo floors and painted their walls and put on additions, no thought was given to the economics of the nursing profession, and nurses today are being paid incredible salaries—$60.00 a month and maintenance, $65.00 a month and maintenance, $70.00 a month and maintenance—having to work

alongside of WPA workers, institutional sudsidiary workers of the WPA, and the nurses' aides of the NYA, who without any training get $50.00 a month and maintenance.

Throughout this country we are having a shortage of nurses who will not nurse in hospitals, and we cannot keep good floor nurses in hospitals, because some industrialist comes in and says, "Are you well paid here?"

She says, "I get $65.00 a month and maintenance."

He says, "Well, when I am out of here and back at my office, you come and see me. We employ industrial nurses, and we pay $150.00 a month."

Nursing is up against big business today, and it is suffering in some places throughout our country in recruitment of nurses for training schools. Why should a nurse pay tuition in a nurses' training school and work three years for nothing, when she can go to a defense industry and begin at $35.00 or $40.00 a week and go up to $60.00 a week for putting little rivets together? Why should she want to pay tuition and work for nothing for a period of three years?

Again I say, "Nursing is up against big business."

I am speaking to you pediatricians who come in very close contact with mothers, through their children, and I say to you that you have a great responsibility to help in this war emergency in trying to enlist into the volunteer nurses' aide groups of the American Red Cross a sufficient number of these women who are overprivileged (and many of your mothers are), who have older children and who are free to take the volunteer nurses' aide training. Because, unless I am very much mistaken, when the Army and the Navy get the numbers of nurses they want, we are going to have a greater shortage than we have today. Keep in mind, gentlemen, when England was in her greatest trouble, there were four volunteer nurses' aides to every one graduate nurse serving the civilian population.

The time is fast coming in our hospitals where the menial jobs, such as carrying trays, acting as receptionists, dressing and undressing patients, making beds, cleaning up the operating room, feeding invalids, feeding people who cannot feed themselves, and a lot of other tasks, can be performed by volunteer nurses' aides thus relieving a graduate nurse for the more skilled duties she is better qualified to perform, such as in the operating room, making charts, taking temperatures, giving medicines and things of that sort that are not entrusted to volunteer nurses' aides. We must rely upon the type of women who you gentlemen contact, because these women as volunteer nurses' aides must work for nothing, and they work always under a graduate nurse. The time is coming, in the very near future, when our hospitals must rely more than they are today on these volunteer nurses' aides.

I need not tell you that these aides get thirty-five hours' training in the chapter house of the Red Cross and the balance of eighty hours in the hospitals, usually in the wards or semiprivate accommodations. They must give 150 hours a year after that, always, as I said in hospitals or doing public health work, public school work, visiting nurses' work, and what not, always under the supervision of a graduate nurse. The service of these volunteer nurses' aides will be indispensable in the future.

What are you gentlemen going to do who remain at home with more internes and housemen on the wane, when cheap labor for hospitals is not going to be as available even as it is today, and today it is very much less available than it was six months ago, with more inexperienced and fewer attendants? You have an added responsibility also to help man our emergency base hospitals for convalescent patients, because the only solution we see in making available beds in our present hospitals in the future in our large defense areas is to have emergency base hospitals, whereby we may place convalescent patients in those hospitals in order to make way for emergency cases, acute surgical cases, etc.

Gentlemen, whether you go to the army or remain at home, our time is a "crisis in history." The old order no longer serves society. Whether you like it or not, it is being replaced. It is demanded by the masses. It is ordered by the common people. It is a world condition.

The forces of reaction are struggling to control these processes of change, attempting to stay what cannot be stayed. We have shut our ears to those who were fed to the monsters in Ethiopia, in China, in Spain, and throughout the world, and today we are paying with the blood of our children for our blunders, our selfishness, our stupidity, and our heedlessness.

Two months ago, in the northern part of this state, I addressed two county medical societies, one of physicians and the other of dentists, a combined group. The first man on the program spoke for forty-five minutes on how to make out wills. What kind of will shall I have to protect my wife and children and my unborn child? The principal emphasis was on how much can I save in taxes in making out this will?

The second man on the program spoke for forty-five minutes on what kind of insurance people should have to protect their wives, to protect their children, and to protect their unborn child.

It was a marvelous build-up for a talk on the Office of Civilian Defense, because I was obliged to tell these gentlemen that unless we won this war it did not make a bit of difference what kind of insurance one had or what kind of will one made, they were not worth the paper they were written on, and you could take them and throw them in the river.

Everybody today wants offensive warfare. Too frequently the people who speak the loudest are doing the least. They want the Army and the Navy to be on the offensive, but they want to remain on the defensive. I am here to tell you, friends, that offensive warfare and victory are much like charity, they begin at home. At home!

And your interest in war, the impression that you leave with that young conscriptee, who leaves his family, a family that has not deprived itself of anything, the man who leaves the community where night life is going on as it always has, I wonder if you have thought of the mental hygiene effect on that boy, where probably nobody but his mother and father knows he has gone, where communities have failed to give any recognition of the sacrifice he is expected to make, even of his life, if necessary.

What we need is more positive and concerted action. Support of the Army and Navy, of course. One hundred per cent. But also discourage the great amount of popular criticism that is going around today, criticism of the OCD, criticism of Federal Security, criticism of the American Red Cross, as to what it did or did not do in Podunk in a flood six months or ten years ago. All kinds of criticism, but little constructive criticism.

Our responsibility is to challenge the enemies of democracy, and we have no moral right to ask these men who are going into the armed forces to fight for something that we are unwilling to fight for ourselves, and that is democracy.

So help, my friends, to create a united front, that the world and civilization may be saved, for the betterment and for the hope of mankind, and to the glory of God.

American Academy of Pediatrics

Proceedings

ELEVENTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

BOSTON, MASS.—OCT. 9-11, 1941

Round Table Discussion on Diabetes

Chairman: Julian D. Boyd, M.D., Iowa City, Iowa.

Associates: L. H. Newburgh, M.D., Professor Clinical Investigation, University of Michigan Medical School, Ann Arbor, Mich.

Priscilla White, M.D., Instructor in Pediatrics, Tufts College Medical School; Physician, New England Deaconess Hospital, Boston, Mass.

Secretary: James W. Bruce, M.D., Louisville, Ky.

DR. NEWBURGH.—While all of you as pediatricians are familiar with the characteristics of diabetes as it occurs in the child, nevertheless I think it is worth while to take a moment in order to point out again the difference between the disease in the young as contrasted with it in the middle-aged and older patients. Diabetes is very much more common in adults than it is in children. Two-thirds of the older patients are obese when the diabetes is first discovered. The diabetic child is usually underweight. In him the disease is severe and ketosis is common. In the older group the diabetes is much milder and ketosis is usually not important. In spite of the greater severity, the diabetic child avoids most of the complications that beset the older people. Perhaps most striking of all is the absence of definite characteristic pathology of the islands of Langerhans in the children. The differences between the two groups are so great that I, personally, am coming more and more to believe that we are dealing with two diseases, not one. A major dietary objective among the adults is reduction of weight. In the children the feeding is centered about the necessity of prescribing an entirely adequate diet from the point of view of protein, calcium, iron, and the vitamins. You will see then that the problem of juvenile diabetes is quite different from that of the adult one.

If I am correct in my view that the disease in the child is fundamentally different from that in the adult, it becomes necessary to find an adequate explanation for each rather than to try to attribute both of them to the same cause. Since you are a group of pediaricians, I need not further discuss the adult patient.

The etiology of the juvenile diabetic is still obscure. While the removal of the pancreas from the experimental animal produces a picture that is sufficiently similar to diabetes in the young to make one believe that the youthful patient is

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suffering from failure of the island cells to produce insulin, nevertheless it is disquieting to be unable to find anything wrong with the specific cells in the vast majority of such patients who come to autopsy. When I say anything wrong, I mean specifically wrong. The studies of Shields, Warren, and others have made it clear that the cellular changes in the islands are not specific. The post-mortem examination only rarely permits the pathologist to say, "This child has died of diabetes mellitus." Even though the microscope has not shown what had been anticipated, nevertheless it is still tenable that the cells are secreting too little insulin. There is some support for this view in experiments carried out by Best and his group. The insulin content of the pancreas of the diabetic was compared with that of the normal, and it was found that there was very much less insulin in the case of the patients. One would infer from these facts that the diabetics were unable to produce insulin at a satisfactory rate. But one needs to be cautious about drawing conclusions from these data, because the same workers have also shown that the insulin content of the pancreas can be lowered by the administration of insulin, as would have been done in the case of the patients. Furthermore, the insulin content of the pancreas was shown to be closely related to the carbohydrate content of the diet by these same workers. When the experimental animal was fed a very small amount of carbohydrate, or when he fasted, there was about one-fourth as much insulin per gram of pancreas as was found in the animal normally fed.

If it is true that the island cells of the diabetic produce too little insulin, is this because there is something primarily wrong with these cells, or because they are not receiving normal stimulation from some other endocrine gland? The hormones of the anterior pituitary have been thought of in this connection, but no positive information is at present available.

For the present we must admit that we are lacking an adequate explanation for juvenile diabetes and must accordingly do what doctors have always done, work out a treatment for the diabetic as best we can in the absence of full etiologic information. I have already mentioned the necessity of being certain that diabetic children receive the full requirement of all the essential dietary substances. This is as important as the regulation of the carbohydrate of the diet. The essential point in regard to carbohydrate is to assure oxidation of a sufficient amount of it to avoid ketosis. More is not necessary. While a more pleasant diet may be constructed with plentiful carbohydrate, this is a secondary matter. It is much more important to lessen the requirement of insulin by restricting the carbohydrate than it is to order a high carbohydrate diet, if the latter is accompanied by wide swings in the blood sugar which result in hypoglycemic attacks, on the one hand, and periods of hyperglycemia on the other. Both states are harmful. It is perhaps easier to recognize the danger done by hypoglycemia than it is to evaluate the effect of the excess blood sugar. It is now certain that hypoglycemia, even of lesser degree, will cause debility and mental sluggishness. More prolonged and deeper hypoglycemia results in organic injury to the brain, which may produce permanent dementia or even death.

Recent studies have convinced me that high blood sugars are also to be avoided. For example, Young has produced permanent diabetes in the dog by the injection of anterior pituitary extract. From the beginning the animal exhibited abnormally high blood sugar. If the latter is avoided by the simultaneous use of insulin, or by diet low in carbohydrate, or by fasting, or by keeping the blood sugar down through the use of phlorhizin, diabetes is not produced. Thus, any method that avoids hyperglycemia prevents the occurrence of this experimental diabetes. On the other hand, the hyperglycemia produced by the pituitary extract will cause permanent injury of the island tissue within a period of as short as two weeks. It seems to me that we can no longer trifle with hyperglycemia in our patients, and

since diabetics frequently exhibit marked hyperglycemia even though there is no glycosuria, I will not be satisfied until I have shown that the blood sugar is continuously within the normal range.

DR. WHITE.—The specific plan for management of the juvenile diabetic patient in our clinic includes hospitalization for education and regulation, a period of one to two weeks; monthly office visits for a year, quarterly thereafter; and an annual check-up at the hospital or summer camp. The principles of treatment which we stress are regulation of diet, administration of insulin, and adjustment of exercise.

Dietary Management.—In the dietary management of the juvenile patient the caloric prescription must be adequate for growth. Calories may be prescribed most scientifically by surface area, more practically by ideal weight, actual height, or age. Of these methods, I personally prefer calories by age; namely, 1,000 at the age of 1 yr., adding 100 per each year of age until the completion of growth and development. To avoid female adolescent obesity, a really serious problem, the caloric prescription for the girl is reduced at maturity to 30 to 40 calories per kilogram of ideal body weight. With boys, who do not have this problem, the calories reach 2,500 to 3,000.

The partition of the diet into its component parts really depends upon one of two schools of thought. If the student of diabetes believes that stimulation of the pancreas alleviates the course of the disease, he will prescribe a diet high in carbohydrate. If he believes that rest of the pancreas alleviates the course of the disease, he will prescribe a diet low in carbohydrate and high in protein and fat. Since 1922, clinicians have reported good results with both types of diet. Up to 1938 there was little in laboratory medicine to favor one type of diet over the other. Young's experiments, however, showed that stimulation of the pancreas by anterior pituitary extract resulted in exhaustion of insulin and finally degeneration of islets. Best and his co-workers showed that rest of the pancreas by insulin, starvation, and low-carbohydrate diets prevented islet degeneration and favored its regeneration, and Lukens showed that any method which lowers blood sugar reverses experimental diabetes. These experiments favor the use of the type of diet so long advocated by Dr. Newburgh; namely, low in carbohydrate and high in fat. Naturally we ask, "How can we reconcile the conflicting clinical reports?" Undoubtedly the duration of diabetes prior to the inauguration of treatment plus insulin therapy are important factors, and theoretically the low-carbohydrate diets have their greatest value in the earliest stages of the disease.

Our choice of diet for the child is a moderate one. We prescribe carbohydrate, protein, and fat in gram ratios 2:1:1, or, in percentages, carbohydrate, 40 per cent; protein, 20 per cent; fat, 40 per cent of the total calories. Thirty grams of carbohydrate are subtracted from the total figure and administered as small lunches before the noon and evening meals and at bedtime, the carbohydrate for the major means being divided as 1/5, 2/5, 2/5, or even as thirds.

Vitamins A, B, and D are usually added (not for diabetes but for general nutrition.

Insulin.—There is no question as to whether or not insulin should be used in the management of the juvenile diabetic. As every one knows, the 100 per cent mortality of the preinsulin era answered the question in the affirmative. The most up-to-date rule is not only insulin from the day of recognition but insulin from the day of onset of diabetes, or, if it were possible, in the prediabetic childhood stage.

Today's question concerns the type of insulin to employ, slowly or rapidly acting insulin or a combination of the two.

TABLE I

TYPE OF INSULIN	SOURCE	REACTION	ZINC	AVAILABILITY (HR.)	DURATION (HR.)	RELIABILITY	HYPOGLYCEMIA	INDURATION	ATROPHY	ALLERGY
Regular insulin	Pancreas	3	+	<1	6	++++	++++	++++	++++	++
Crystalline insulin	Pancreas	3	+	<1	8	++++	++++	++	++++	+
Protamine zinc insulin	Sperm	7	+++	6-8	24-72	+++	++++	+	++++	++++
Protamine zinc (clear) insulin	Sperm	3	+++	2	18	+	++++	0	0	0
Globin	Red blood cells	3	+++	2	24	+++	++++	0	0	0
Histone	Thymus	7	++	<1	24+	++++	++	0	0	0

Before considering the relative merits of the various insulins, commercial and experimental, let us consider the properties of an ideal insulin:

1. Its availability should be within an hour of administration.
2. Its action should be for twenty-four hours, not more, not less.
3. It should be reliable (the same action day in and day out).
4. The reaction should be neutral.
5. Its physical property clear rather than turbid.
6. The release of insulin so constant and steady that hypoglycemia is avoided.
7. It should be nonirritating from the point of view of urticaria, lipodystrophy, and induration.

Table I shows the comparison of insulins under investigation, and it is at once apparent that histone is the high-ranking one. This work is to be published in detail by Dr. C. Cabell Bailey and Major Alexander Marble of our clinic.

Therefore we must consider our routine and our special studies in 1941.

From 1935 to 1941, the juvenile patients have been divided into two groups according to duration of diabetes. The initial dose of insulin for the short duration case is based on age: under 5 years, 10 units; between 5 and 10 years, 20 units; between 10 and 15 years of age, 30 units. The case of long duration receives the usual breakfast dose of rapidly acting insulin along with twice that dose of protamine zinc insulin given separately but simultaneously. We have not been successful in mixing the two in one syringe. Readjustments are made in either case on premeal and retiring specimens. The rapid insulin is daytime insulin, the slow insulin is nighttime insulin.

The diet is constant, the insulin the variable with protamine zinc insulin. With histone and others the insulin is the constant, the diet the variable. There are two arguments against histone: The new patient is not adequately trained in emergency, rapid insulin, and the lack of 72° storage may increase our incidence of juvenile coma, but the trend for improved insulin and total treatment is evident.

Our standard for treatment is similar to that of Dr. Boyd and Dr. Newburgh: normal blood sugar before meals, glycosuria less than 5 per cent of the carbohydrate intake, freedom from symptoms, normal cholesterol, normal weight, and freedom from ketosis.

CHAIRMAN BOYD.—Usually diabetes mellitus is not considered a disease of childhood, yet is frequently makes its appearance during that period of life. More commonly its onset is during adulthood. Probably for this reason, the specialists in its management usually are internists rather than pediatrists. From the standpoint of the young patient this is unfortunate. About 10 per cent of patients with diabetes develop their symptoms at some time during the first two decades, when problems relating to childhood and to maturation are of great importance. Unless such problems are given proper consideration in the plan of treatment, the patient will be harmed and the effectiveness of therapy will be lessened. There is a tendency to treat the diabetes rather than the child, without recognition of the special needs which childhood imposes. The usual current regimen of treatment, which often is applied without consideration of the age of the patient, is based on experience with adult patients. Articles in our medical journals and texts dealing with diabetes usually are written with the adult patient in mind, and if the child is mentioned at all, the reference as a rule is casual and meager. The standards for adequacy of treatment commonly employed may be adaptable to the adult patient's needs yet be insufficient to control the diabetic state in the child. For these and for other reasons it is important that pediatric philosophy be adopted and utilized in treating all

young patients with diabetes. Such consideration should be extended not only throughout childhood but throughout adolescence as well.

The basic principle of pediatric practice is different from that of the internist. The pediatrist is interested in the problems of the child as they are affected by health or disease rather than in the characteristics of diseases in themselves. We feel it important that all plans of therapy be designed to safeguard the normal development of the child as well as to conserve his health. Possibly there is no disease in which such consideration is needed more than for the child with diabetes mellitus. Diabetes may be considered as an underlying metabolic anomaly rather than as a disease; once established, it remains as a limiting factor in the body's functional capacity for the remainder of life. Despite its incurability, however, it need not serve as an insuperable handicap; if the individual with diabetes can be kept under a regimen fully suited to his diabetic condition, he may look forward with fair confidence to a life of comfort, usefulness, and enjoyment. Under such control, the child with diabetes need not be handicapped in his growth and development. On the other hand, a poorly designed regimen of management may fail to conserve his health and capacity and may make life a chore rather than a privilege. For the child, the program of treatment should be designed so as to permit consummation of all the functions belonging to childhood; if not, the patient will be correspondingly handicapped not only during his childhood but similarly during his adult life.

Comparing the usual regimen of diabetic management as designed for the adult patient with that needed for the welfare of the child diabetic certain distinctions are outstanding. The usual pattern of treatment is passive: it is designed more to meet the patient's personal demands than it is to insure his continued well-being. It is no more exacting than is necessary to avoid frank evidence of disease or disability. Possibly such a routine is proper for the elderly patient who is seeking comfort alone. On the other hand, such a passive regimen fails decidedly to conserve the child's resources for subsequent health and normal existence and may be expected to lead ultimately to a poor outcome as compared with that obtainable through careful management.

Before insulin became available, the problem of the child with diabetes was stereotyped and of brief duration. Fatal complications could be postponed only through the maintenance of marked undernutrition. Under such treatment, the child lived a miserable existence, was dwarfed, was subject to degenerative lesions of important organs, and usually ended his existence when acidosis supervened in spite of rigorous starvation. In no way could he approximate a normal child, and he lived a life of invalidism. Availability of insulin has changed the whole nature of the problem. Now it is easy to keep the diabetic child alive through the use of insulin, even though the level of control of the diabetes be poor at all times. Maintenance of life is so easy with insulin therapy that little medical skill is necessary once a regimen in any degree adequate has been instituted. With a little initial training the members of the diabetic patient's household are able to care for him with minimum medical assistance and from apparent results may be led to feel that everything necessary or possible is being offered the patient. In this regard, insulin therapy works against the diabetic child's best interests; it permits the continuance of unsatisfactory levels of control without recognition of their inadequacy.

It no longer is sufficient to think in terms of prevention or postponement of death of the diabetic child. It is not enough to maintain him in any stage less than one of buoyant health. Techniques are available to insure the diabetic child of such excellent control of his metabolic anomaly that his handicap need not seriously affect his health or his prospects during later life. A favorable outcome, however, requires not only the establishment of a suitable regimen initially, but its continuance

throughout the duration of life. There is no great virtue in treating the diabetic child at the outset of his illness in a manner which may rescue him from acidosis but which will start him on a path of continuous compromise with disaster. It is not much better to assist in the establishment of a regimen which passively is good but which will not protect him from degenerative changes or which will fail him when he meets with unusual stresses. Any desirable standard for management of diabetes in the child should be designed to conserve his physical resources in the fullest degree while holding his diabetes in check. It should be such that the child's development and maturation in all regards will be fostered. Moreover, the goal should be progressive; it should not relate merely to the immediate future but should be adapted periodically to the advancing medical and social needs of the child.

Our definition of adequate control of diabetes mellitus is based on the approximation of normal physiologic conditions in so far as they can be attained. The desirable regimen is one which will assure adequate nutrition, with avoidance of hyperglycemia or glycosuria at all times. While this ideal may not be reached, any compromise with it should not be made without sufficient reason. Tables I and II illustrate the various levels of diabetic management or mismanagement, the laboratory findings which characterize them, and the interpretation of each.

TABLE I.

LEVELS OF CONTROL OF DIABETES MELLITUS

LABORATORY FINDINGS		DESIGNATION OF LEVEL OF CONTROL	REMARKS
Blood sugar Glycosuria Nutrition	Normal None Optimum	Excellent	Goal of therapy; approximation of normal status
Hyperglycemia Glycosuria	Infrequent, minimal Infrequent, mild	Good	Attainable in patient initially well stabilized; maintainable if free from nondiabetic complications, and under periodic medical and social supervision
Hyperglycemia Glycosuria	Recurrent Intermittent, mild	Fair	Readily attainable, interspersed with good or of excellent control, if facilities are good
Hyperglycemia Glycosuria	Fairly constant; varying degree Frequent or continuous; mild	Poor	Approaches noncontrol; compatible with apparent passable health, but a forerunner of serious complications

Certain facilities are essential for the successful management of diabetes in the child. These include skilled medical, dietetic, laboratory, and hospital services during the period when the patient is undergoing stabilization. In the home there must be provisions for serving the carefully prescribed diet quantitatively, for insulin administration, and for frequent urinalysis. Arrangements must be made to insure continuous availability of insulin and other equipment and supplies. The patient's status should be reviewed by the physician at least twice a year and preferably more often throughout childhood and adolescence, so that the regimen may be adjusted to the current state of growth, abnormalities be detected, and complications avoided.

The successful management of diabetes in the child requires attention to certain factors which lie beyond the field of medicine. The importance of some of these may outweigh that of medical care itself, in relation to the patient's ability to follow the prescribed routine. The physician frequently must take and maintain the re-

sponsibility for matters relating to the economic and social welfare of these young patients. No one other than the physician has the ability to correlate such problems with the child's medical needs and to interpret them to others.

TABLE II

LEVELS OF NONCONTROL OF DIABETES MELLITUS

LABORATORY FINDINGS		DESIGNATED LEVEL OF NONCONTROL	REMARKS
Glycosuria	Periodic, marked, but only for short intervals	Noncontrol, temporary	Episode during course of better management, due to lapse of therapy or to intercurrent infection; predisposes to chronic noncontrol
Glycosuria	Continuous, marked, may be ignored; buffered through insulin injections	Noncontrol, chronic masked	Status incompatible with patient's ultimate welfare; leads toward degenerative states; may be without symptoms, and pass for satisfactory control
Glycosuria	Continuous, unmodified through dietary or insulin therapy	Noncontrol, chronic, not treated	Predictable forerunner of severe complications, sequelae, death

The cost of the routine of diabetic management goes beyond the doctor's professional fees and those of the hospital and laboratory. The raw ingredients for a satisfactory diet for the diabetic child will cost in excess of two dollars a week. With the average insulin need, the cost of insulin, testing solution, and other sundries will equal a dollar or more weekly. The scales, syringes, and other equipment needed for diabetic care will cost about fifteen dollars. While these amounts may seem trifling, the continued costs comprise a drain on the family's resources. When professional and hospital fees are added, the maintenance of suitable treatment throughout the years may impoverish a middle-class family. Many families find it a catastrophe from the start; probably the majority of diabetic children come from the homes of the medically indigent. Any regimen of therapy which we agree is necessary for the diabetic child should be prescribed for the poor as well as for those who can afford to ignore cost. Can the physician justify himself in prescribing a low-cost regimen, when he knows that it will serve to temporize only, and eventually will fail utterly to meet the patient's needs? On the other hand, can he justifiably prescribe the needed regimen which is beyond financial reach of the family, and then do nothing to help the family to meet the situation? There is no ready answer for such a problem. However, when one considers the salvageability of the diabetic child under proper care versus the predictably bad results with a poor regimen, it seems a matter of social economy to invest in the care of the diabetic child. It is better to help in making the patient self-sufficient and healthy than to impose a routine which will lead to progressively greater dependency. The well-qualified and specially trained medical social worker is a valuable aid in the interpretation of the problems of diabetes to the family and to community agencies, and frequently she can find a solution when the problem has seemed desperate.

The child with diabetes mellitus needs his schooling even more than does the child without affliction. With good preliminary training and with proper control of his diabetes, he has the capacity to become a useful adult member of his community. Without schooling, he may become a social liability even though his diabetes has been held in check. Frequently it is necessary for minor adjustments of the school

routine to be provided by the school authorities, so that the child's diabetic needs can be met. The physician should help the parents to make the necessary arrangements and aid in interpreting the child's status and limitations to the teacher.

In line with this problem of education, it is important that the parents and the patient be assisted in making a proper emotional adjustment to the child's condition and that a proper attitude be maintained. At the outset the parents should learn the nature of diabetes, what may be expected with good and with poor treatment, and the part they must play in treating the child. An important part of the parent's responsibility is to create and maintain a proper state of mind regarding it. The parents must be brought to face the reality of the condition and to accept it; then and only then will they be able to help the child make a similar adjustment. In general, the child is less of a problem than the parents. The child who is encouraged to conceal his diabetic condition from school authorities and from his companions will build up an unnecessary barrier to his own best management. No great regimentation is necessary for the daily control of diabetes: the child and his parents should accept as a matter of course that only the prescribed foods may be eaten, and that insulin must be used regularly in accordance with his needs; they should recognize that this is a small price to pay for the excellent health which the well-controlled patient can enjoy. The child who is shielded and overprotected because of his disease is being forced into continued dependency on others; usually this state will be carried over into adult life, and it may prove an insuperable barrier to proper social adjustment and to happiness. On the other hand, the adolescent patient may revolt not only against parental authority, but in addition may relax or abandon the routine of diabetic control which has protected him during his earlier diabetic experience. The wise physician will foresee these emotional difficulties and often will help the patient avoid them through suitable measures of mental hygiene.

Plans for the diabetic child's future should be made well in advance. The need for training for self-sufficiency has been mentioned. This is as important for the girl as for the boy. Diabetes mellitus carries with it many factors which serve as an obstacle to successful marriage; it is not right for the girl with diabetes to look forward to marriage as an answer to her problems. Even without consideration for the eugenic aspects of diabetes, the physician should caution the diabetic young person against marriage unless social and economic as well as emotional harmony are assured.

The physician may well raise the question as to his qualifications to treat diabetes in the child if all the points discussed are to be met. None of us is qualified for the job; but sometimes we cannot pass it on to anyone else better qualified. We must make use of the facilities we have and do the best job our abilities and those facilities permit. It is proper that we be humble as to our qualifications, however, and that we feel neglectful if we have failed to use any available resource which would further the prospects for the diabetic child.

DISCUSSION

DR. H. P. FINE, PERTH AMBOY, N. J.—Should all foods in the diabetic diet be prescribed and weighed, or are reasonably accurate household measurements sufficient once the diet has been stabilized?

CHAIRMAN BOYD.—The diet should be quantitatively prescribed and administered. Accurate measurement of volume may be used as a substitute for weighing of appropriate foods. With prolonged experience in weighing of specific foods, the patient or attendant may gain sufficient skill to permit fair accuracy through measurement rather than weighing.

DR. W. L. FUNKHOUSER, ATLANTA, GA.—What is your attitude toward the use of the "free diet" covered through the use of insulin?

DR. WHITE.—The "free" diet is not constant, and the success of any diabetic diet is based on its constancy. The newer animal experiments indicate that stimulation of the pancreas favors degeneration, whereas rest of the pancreas favors regeneration. We know that a free diet is one high in carbohydrate, hence will serve to stimulate the pancreas. This is another argument against its use.

CHAIRMAN NEWBURGH.—The diet should be prescribed quantitatively and enforced.

CHAIRMAN BOYD.—We stress the desirability of aglycosuria. This state is difficult or impossible to attain with the diabetic child whose diet is not quantitatively administered. After a weighed diet has been followed conscientiously for several years the patient who relaxes his vigilance may feel that he is following a free diet, yet he may be following quite closely the pattern of his earlier prescribed diet. It is plain that an unrestricted free diet may vary widely as to its nature and relative constancy; the insulin requirement similarly will vary. This prevents the excellence of control which we feel is essential for the patient's best interests. For still another reason the free diet is not to be recommended. This relates to the importance of meeting the optimal nutritional state of the child, whether or not he has diabetes mellitus. Unless a prescribed regimen designed particularly for optimal nutrition is observed, the child's best interests are not conserved.

DR. I. MCQUARRIE, MINNEAPOLIS.—I feel that the use of the free diet leads to lowered tolerance.

DR. RICHARD WAGNER, BOSTON.—Some doctors have obtained good results using the free diet. There are various kinds of diabetic patients. Under similar management some do well and others do badly.

DR. W. C. A. STEFFEN, FLUSHING, N. Y.—Do you think that diabetes gets worse as the child gets older, or do you think the progressive insulin requirement is due to faulty management?

DR. NEWBURGH.—No. The disease progresses for a short time after its onset and then becomes stabilized. It remains at this level if treatment is satisfactory, barring the effect of infection.

DR. WHITE.—After the third year the ratio of units of insulin per kilogram of body weight does not increase. I think the increase in severity is due more to the factors which control growth and development than to faulty diabetic management.

CHAIRMAN BOYD.—In our clinic, Doctor Jackson has found that diabetic children who maintain an excellent level of control throughout their disease do not require increasing amounts of insulin with the passage of time, except to cover the increased food intake. When the disease is recognized early and when complete control is instituted immediately and maintained at all times, the patient's insulin needs do not advance and he will exhibit a wide margin of stability. A number of his patients continue to show gradual improvement rather than progression during the first few years of their disease. However, patients who have been poorly regulated for months prior to stabilization have less recovery of tolerance and a narrower level of stability. Whether the early months of the disease are characterized by advance of retrogression of insulin needs seems dependent on adequacy of control.

DR. H. C. THOMPSON, JR., TUCSON, ARIZ.—Should one try to avoid giving insulin after having given it for a long period of time in the patient who has been doing very well?

DR. WHITE.—If the patient has clinical symptoms of diabetes, one should never try to get along without insulin.

CHAIRMAN BOYD.—Practically all diabetic children must continue the use of insulin indefinitely if gross glycosuria is to be avoided. Even in the exceptional patient who has reached a state of tolerance following prolonged and excellent management which makes the further use of insulin seem unnecessary, we have preferred to continue its use with minimum dosage rather than to discontinue it entirely. There are several reasons for this policy. One relates to the subsequent need for insulin which most such patients will exhibit spontaneously within a period of weeks or of months. Another concerns itself with the demand for insulin at times of infectious disease or other complication. The third has to do with the mental attitude of the parents; it seems better for morale if the parents face once and for all the fact that insulin will be required in the management of the diabetic child, rather than to be offered a faint and probably false hope that after a time insulin no longer will be needed.

DR. D. B. LANDAU, HANNIBAL, MO.—Do considerable changes in insulin dosage have to be made when the child returns to school in the fall and also when there is a change in the child's amount of exercise?

DR. WHITE.—Exercise in controlled diabetes prevents glycosuria and lessens the requirement for insulin; in the uncontrolled diabetic, on the other hand, it increases glycosuria. With the decrease in exercise resulting from return to school, insulin requirement increases. I do not know of any good scientific evidence that emotional strain affects glycosuria and insulin need.

DR. NEWBURGH.—Physical exercise increases the utilization of glucose by the diabetic, hence the insulin requirement at such times is lessened.

CHAIRMAN BOYD.—In the diabetic patient who is well controlled basically, emotional stress and level of exercise remain as major factors which can affect his response. We feel that emotion can alter insulin need. Glycosuria has resulted from that apparent cause; appetite has been affected, and even vomiting and diarrhea have been noted. Psychologic factors play an important part in maintaining suitable control of diabetes in the child. Unless the physician is equipped to cope with problems of mental hygiene of the child patient and of the family, he cannot offer the fullest service necessary for the diabetic child's welfare. Presumably a pediatrist will have such attributes.

We agree with Doctors White and Newburgh as to the effect of exercise on sugar utilization. During the period of hospitalization it is our policy to control the child's physical activity as well as possible and to adjust for variations through alteration of insulin dosage. In the home it probably is more satisfactory to administer measured amounts of fruits to compensate for unusual episodes of physical activity. The insulin need of some of our subjects has declined as much as 50 per cent during summer vacation.

DR. C. E. WARD, JACKSON, MISS.—We have felt that the average diabetic child can be controlled satisfactorily through urine examinations, following Wilder's plan. What is your opinion of this?

CHAIRMAN BOYD.—May I ask Doctor Jackson of our clinic, to answer this question?

DR. JACKSON, IOWA CITY.—The foregoing discussion has brought out the importance of thorough control of diabetes at the earliest moment and the maintenance of that state in so far as possible. We feel that initially a prolonged period of hospitalization is important if optimum conditions are to be established. Usually from six to eight weeks are needed to attain stability. Under hospital routine, with a specially trained staff, it has seemed possible to gauge progress of control on the basis of urinalysis and evidence of mild hypoglycemia. Blood sugar determinations have seemed most useful as the termination of stabilization is approached. In the home, urinalysis serves as an adequate guide. Recurrent periods of observation in a hospital or under equivalent control is important at intervals of six months or less throughout childhood to assure the constancy of the desired level of control.

DR. WHITE.—It is feasible to treat the diabetic child without blood sugar analyses on the basis of urine examinations only.

DR. NEWBURGH.—Some diabetics acquire a high threshold. They may have hyperglycemia without glycosuria. When the treatment has resulted in continuous absence of sugar from the urine, the adequacy of regulation must be checked by demonstratedly normal blood sugar levels.

DR. NEWBURGH, ANN ARBOR.—What late effects have you seen which you could attribute to prolonged hyperglycemia?

CHAIRMAN BOYD.—Instances of degenerative disease in our patients have been confined to those who had been poorly controlled. Such degenerative changes have included dwarfism, hepatomegaly, changes in the retina or optic nerve, and clinical cataract. Recently we have reported the coincidence of precataractous lens changes (posterior subcapsular opacities, as revealed by the slit lamp and biomicroscope) with periods of prolonged hyperglycemia. With resumption of better levels of control, these opacities have not advanced for periods of years. It seems reasonable to assume that prolonged hyperglycemia affects many body tissues adversely.

DR. JACKSON.—The most notable apparent effect of prolonged hyperglycemia is evidenced by the difference in response of patients who recently have become diabetic to those who have remained glycosuric for some time before stabilization is attempted. The latter group has a much narrower zone of stability and definitely is more difficult to control than patients who have been well regulated soon after the onset of their disease.

DR. W. E. NELSON, PHILADELPHIA.—Can a child who is excreting 5 to 10 Gm. of sugar daily gain properly?

CHAIRMAN BOYD.—He cannot. Apparent freedom from gross difficulty does not establish the harmlessness of prolonged glycosuria. Before sugar appears in the urine, the body's mechanisms will have attempted to avoid glycosuria. If sugar appears, it offers evidence that these mechanisms have been subjected to strain and that they have failed to meet the situation in a normal manner. This comprises a break in compensation of a vital function, and in my mind it implies insult to that function with exhaustion of its reserves. If repeated or continuous, one might expect ultimate loss of recovery of tolerance, as has been described in the diabetic child after two or three years of treatment which countenances glycosuria.

DR. R. E. JENNINGS, EAST ORANGE, N. J.—With intent to prevent development of diabetes in other members of the family, would you try to change the family diet in the home of a child with diabetes in so far as the fat content is concerned?

CHAIRMAN BOYD.—Specifically, no. However, the need for an adequate diet for each member of the household should be stressed. If the type of diet prescribed for the child is used as a basis for the family menus, there will be several advantages. The child will seem more a member of the group and will accept his regimen more readily. The level of health of the remainder of the group should improve if the patient's diet has been designed to meet optimum nutritional needs. In this indirect manner, the development of diabetes in other members of the family may be retarded. I would emphasize not the level of fat, however, but place equal emphasis on all the components of a good diet.

DR. H. T. CRANE, PLAINFIELD, N. J.—What criteria do you use in making a diagnosis of diabetes?

DR. WHITE.—The diagnosis of diabetes either in the child or in the adult patient depends on the demonstration of two abnormal findings, hyperglycemia and glycosuria. Doctor Joslin's criteria are glycosuria plus a fasting blood sugar of 130 if venous, or a postprandial blood sugar of 170 if venous and 200 if capillary.

CHAIRMAN BOYD.—Glycosuria at any time raises the question as to the likelihood of diabetes. It is important, however, to rule out nonsugar reducing substances as a cause for a positive Benedict's test. Such false tests are encountered rather often, especially in the concentrated urine of young infants. The whole day's output must be tested fractionally if glycosuria is to be ruled out beyond question. Sugar tolerance tests may be necessary to rule out transitory glycosuria or hyperglycemia. If such a test reveals a blood sugar curve which rises higher and falls more slowly than in the normal individual, diabetes must be considered likely. Sometimes such findings are observed during the course of infection, but subside later; such persons may become frankly diabetic at a later time, or may not. Familiarity with the microtechnique of blood sugar determination is desirable for anyone dealing with diabetic patients; it is simple, easy, and reliable if properly performed.

DR. G. K. HAGAMAN, ST. PAUL, MINN.—Vitamin B_1 has been called the poor man's insulin. In what way does it help, if this true?

DR. JACKSON.—From an extensive study of five well-controlled diabetic children, we have concluded that the ingestion of vitamin B complex in amounts which exceed those obtainable in well-planned adequate diets did not lessen the insulin requirement.

DR. A. E. FISCHER, NEW YORK CITY.—How do you account for the development of obesity in diabetic adolescent girls who presumably are receiving diets restricted in calories?

CHAIRMAN BOYD.—The laws relating to the conservation of energy apply as much to the adolescent diabetic girl as to anything else. I would assume that children who gain weight under a dietary regimen which designedly is deficient in calories were violating their diet.

DR. NEWBURGH.—Sometimes such violation is nonapparent and unintentional. I recall an instance of a farm girl who was offered choice between various protein foods in her diet and who consistently used pork. The higher fat content of the pork seemed to account for the discrepancy in calories.

DR. McQUARRIE.—What is the effect of infection in diabetes?

CHAIRMAN BOYD.—Even with mild infections, the patient's insulin requirement for his standard diet increases definitely, and sometimes markedly. In part, this may be explained on the basis of lessened exercise. We have seen the insulin

need increased by 20 per cent merely by limiting a diabetic child to bed, without concurrent infection. In my opinion, there is an additional factor, due to the effect of the infection in itself, possibly through the mechanism of the circulating toxins lessening the responsiveness of body tissues. Even in the nondiabetic, some degree of acetonuria is not uncommon with infectious disease.

DR. NELSON.—Will a child who is in good balance, with proper regulation of diet and of insulin, develop coma if he breaks diet?

CHAIRMAN BOYD.—Not abruptly. Time would be required. Concurrent infection could induce it, however.

DR. WHITE.—With the use of protamine insulin it is almost impossible for the child to develop diabetic coma unless he has an overwhelming infection or has omitted the use of insulin.

DR. JESSIE M. BIERMAN, WASHINGTON, D. C.—How can the social factors which Dr. Boyd mentioned as important in the management of the juvenile diabetic be adequately taken care of in private practice?

CHAIRMAN BOYD.—The answer rests with the degree of insight and of initiative which the physician possesses. It is unfortunate that formal medical teaching devotes little or no time to the study of social problems as they affect health and the individual as a whole. The physician who has available the services of a competent assistant with medical-social training is fortunate, and so are his patients. Most of us must do our own social work; however, there are skilled workers in many communities who could be helpful in meeting the social problems of chronic illness if they were requested to do so. The qualified worker can do much of value in the home of plenty; where economic problems are present, her services are invaluable. Referring patients to such trained workers would help in the avoidance of emotional, social, and educational handicaps which otherwise may be expected to develop even in the patient who maintains excellent medical control of his diabetes.

News and Notes

The appended list of Fellows of the American Academy of Pediatrics in service is probably incomplete. The editors will welcome further names of Fellows entering service.

Army

Robert A. Bier, Washington, D. C. (Major)
Max Deutch, St. Louis, Mo. (Captain)
Richard G. Elliott, Lexington, Ky. (Captain)
Warren C. Fargo, Cleveland, Ohio (Lieutenant Colonel)
Seymour Fisher, Springfield, Ill. (Captain)
Moe Goldstein, Forest Hills, L. I., N. Y. (Lieutenant)
G. E. Harrison, Mason City, Iowa (Major)
Albert M. Jones, Memphis, Tenn. (First Lieutenant)
Irving LeBell, New York, N. Y. (Captain)
Harold Lipton, Brooklyn, N. Y. (Captain)
George S. Littell, Dallas, Texas (Major)
Paul R. Meyer, Port Arthur, Texas (Captain)
William A. Reilly, San Francisco, Calif. (Lieutenant Colonel)
Albert F. Stein, Chicago, Ill. (Captain)
Robert A. Strong, New Orleans, La. (Colonel)

We do not have information regarding the rank of the following:

John E. Brown, Jr., Columbus, Ohio
Paul D. Clark, Burlington, Vt.
Nathan H. Einhorn, Philadelphia, Pa.
Merrill W. Everhart, New Orleans, La.
Stanley S. Freedman, Providence, R. I.
Henry N. Pratt, Boston, Mass.
C. Walter Rumpf, Faribault, Minn.
Abraham Tow, New York, N. Y.
Raeburn J. Wharton, Johnson City, N. Y.

Navy

Arthur F. Abt, Chicago, Ill. (Lieutenant Commander)
Edward D. Anderson, Minneapolis, Minn. (Lieutenant Commander)
Arthur P. Black, El Paso, Texas (Lieutenant Commander)
James E. Bowman, Philadelphia, Pa. (Lieutenant)
Sims A. Chapman, New Orleans, La. (Lieutenant Commander)
Enos P. Cook, San Jose, Calif. (Lieutenant Commander)
George L. Drennan, Jacksonville, Ill. (Lieutenant Commander)
R. Cannon Eley, Boston, Mass. (Lieutenant Commander)
John K. Glen, Houston, Texas (Lieutenant Commander)
John C. McKitterick, Burlington, Iowa (Lieutenant Commander)
Joseph Palma, Honolulu, Hawaii (Lieutenant Commander)
George Lyon, Huntington, W. Va. (Lieutenant Commander)

We do not have information regarding the rank of the following:

Stanley V. Laub, Detroit, Mich.
Newton T. Saxl, New York, N. Y.
Sherl J. Winter, Dayton, Ohio

Red Cross and Other Services

John E. Gordon, Boston, Mass.
Jacob N. Lande, Sioux City, Iowa
Mila I. Pierce, Evanston, Ill.

Canadian Forces

Harry L. Bacal, Montreal, Quebec (Navy)
Aubrey K. Geddes, Montreal, Quebec (Army)
Gordon Manace, Toronto, Ontario (Air Corps)
John R. Ross, Toronto, Ontario (Major)
Frederick F. Tisdall, Toronto, Ontario (Major, Air Corps)

A group of our Central and South American colleagues who had been attending the recent Pan-American Congress on Child Protection in Washington were present at the Region III meeting as guests of the American Academy of Pediatrics. Following the Washington meeting they had been on a tour sponsored by the Kellog Foundation which ended at Cleveland. The guests were welcomed and introduced at the luncheon meeting the first day and were guests of Region III at the banquet on Friday night. The following attended:

Argentina	Dr. Mario H. Bortagaray
Brazil	Dr. Dante Costa
Chile	Dr. Guillermo Morales-Beltrami
	Dr. Arturo Scroggie V.
Colombia	Dr. Hector Pedraza
	Dr. Jorge Camacho Gamba
Cuba	Dr. F. Hurtado
	Dr. Elvira Rey
Ecuador	Dr. Carlos Andrade Marin
El Salvador	Dr. Ranulfo Castro
Mexico	Dr. Hermile L. Castaneda
	Dr. Fernando L. Madero
Peru	Dr. Manuel Salcedo
Panama	Dr. Leopoldo L. Benedetti
Paraguay	Dr. Carlos Ros
Uruguay	Dr. Victor Escardo y Anaya

Dr. Donovan J. McCune of New York has been appointed to the American Board of Pediatrics by the American Pediatric Society to fill a vacancy due to the resignation of Dr. Philip van Ingen who has served on the Board since its formation in 1933.

Comment

The recent meeting of Region III of the American Academy of Pediatrics at Cleveland, May 14, 15, and 16, was designated as "First War Session" by the program committee, and discussion of various aspects of the War theme dominated the meeting. At a luncheon meeting the first day, Dr. Borden Veeder, president-elect, spoke on the "Academy and the War." The program that evening was a discussion of "The Physician (Especially the Pediatrician) and the War," with speakers from the Office of Selective Service Headquarters in Wash-

ington, the Office of the Committee on Procurement and Assignment of the Fifth Corps Area, and the Office of Civilian Defense. The following afternoon the theme was "The Protection of Our Children During the War." Dr. Joseph Stokes, Jr., of Philadelphia spoke on the contagious disease problem, while Dr. Julian Boyd of Iowa City and Dr. Sebrell of Washington discussed the nutritional care and vitamins. Dr. Bert Beverly of Chicago discussed the "Psychological Aspects of Youth and the War" and Dr. Martha Eliot, "The Welfare of Our Children in Wartime." There was also a committee luncheon on National Defense which presented two resolutions relating to the health of children and the pediatrician which were adopted by Region III and ordered sent to the executive committee of the Academy for action at their coming meeting in June. In addition to these more formal talks there was a constant discussion and questioning going on throughout the meeting centering chiefly on "What should I do?" and "What can I best do?"

The speakers from the three governmental bureaus having to do with the placement of personnel answered so many of the questions uppermost in the minds of all that their addresses have been published together in this issue and will be found following the section on Original Communications. The material is so timely that the editors feel our readers who were not present should have this information. The remaining five papers will be published as soon as available.

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